The Effectiveness of Right Heart Catheterization in the Initial Care of Critically Ill Patients

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Objective.—To examine the association between the use of right heart catheterization (RHC) during the first 24 hours of care in the intensive care unit (ICU) and subsequent survival, length of stay, intensity of care, and cost of care.

Design.—Prospective cohort study.

Setting.—Five US teaching hospitals between 1989 and 1994.

Subjects.—A total of 5735 critically ill adult patients receiving care in an ICU for 1 of 9 prespecified disease categories.

Main Outcome Measures.—Survival time, cost of care, intensity of care, and length of stay in the ICU and hospital, determined from the clinical record and from the National Death Index. A propensity score for RHC was constructed using multivariable logistic regression. Case-matching and multivariable regression modeling techniques were used to estimate the association of RHC with specific outcomes after adjusting for treatment selection using the propensity score. Sensitivity analysis was used to estimate the potential effect of an unidentified or missing covariate on the results.

Results.—By case-matching analysis, patients with RHC had an increased 30-day mortality (odds ratio, 1.24; 95% confidence interval, 1.03-1.49). The mean cost (25th, 50th, 75th percentiles) per hospital stay was $49 300 ($17 000, $30 500, $56 600) with RHC and $35 700 ($11 300, $20 600, $39 200) without RHC. Mean length of stay in the ICU was 14.8 (5, 9, 17) days with RHC and 13.0 (4, 7, 14) days without RHC. These findings were all confirmed by multivariable modeling techniques. Subgroup analysis did not reveal any patient group or site for which RHC was associated with improved outcomes. Patients with higher baseline probability of surviving 2 months had the highest relative risk of death following RHC. Sensitivity analysis suggested that a missing covariate would have to increase the risk of death 6-fold and the risk of RHC 6-fold for a true beneficial effect of RHC to be misrepresented as harmful.

Conclusion.—In this observational study of critically ill patients, after adjustment for treatment selection bias, RHC was associated with increased mortality and increased utilization of resources. The cause of this apparent lack of benefit is unclear. The results of this analysis should be confirmed in other observational studies. These findings justify reconsideration of a randomized controlled trial of RHC and may guide patient selection for such a study.

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MANY CARDIOLOGISTS and critical care physicians believe that the direct measurement of cardiac function provided by right heart catheterization (RHC) (also known as pulmonary artery catheterization) is necessary to guide therapy for certain critically ill patients[1-3] and that such management leads to better patient outcomes.[4] While the benefit of RHC has not been demonstrated in a randomized controlled trial (RCT), the popularity of this procedure and the widespread belief that it is beneficial make the performance of an RCT difficult. Physicians cannot ethically participate in such a trial or encourage a patient to participate if convinced the procedure is truly beneficial. The most recent attempt at an RCT was stopped because most physicians refused to allow their patients to be randomized.[5]

For editorial comment see p 916.

In the absence of RCTs of RHC, observational studies have been used to evaluate its effectiveness. The relative risk of death has been found to be higher in the elderly[6] and in patients with acute myocardial infarction[7-9] who were managed with RHC. In a study of acute myocardial infarction in Medicare patients, hospitals with higher than expected use of RHC had higher than expected mortality.[10] In observational studies, however, the decision to use or withhold RHC is left to the discretion of the physician. Thus, treatment selection is confounded with patient factors that are also related to outcomes. For example, patients with low blood pressure are more likely to be managed with RHC, and such patients are also more likely to die. The effect of such treatment selection bias has been called "confounding by indication."[11] Most of the studies cited were not able to adjust comprehensively for the variety of factors that influence the selection of patients for RHC.

To adjust for treatment selection bias, the variables that independently affect the decision to use or withhold the treatment must be identified and measured. A statistical adjustment is then made to account for their estimated effect on the treatment decision. The propensity score, described by Rosenbaum and Rubin,[12,13] is a powerful method of accounting for these factors and adjusting for treatment selection bias. To calculate the propensity score, all known variables that may influence the decision to perform a procedure are included in a multivariable logistic regression analysis that determines the probability that the procedure will be performed. This probability is called the propensity score, with a higher score indicating a higher probability of receiving the treatment. The association of the procedure with an outcome can then be estimated after adjusting for treatment selection bias using this propensity score. In effect, this technique enables us to assess the association of RHC with specific outcomes in patients with an equal probability of receiving the procedure.

The purpose of this study was to use the propensity technique to evaluate the association of RHC performed during the initial 24 hours of an ICU stay with subsequent survival, length of stay, intensity of care, and cost of care in a large cohort of critically ill patients and in predefined patient subgroups.

METHODS

The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) was a 5-center study of decision making and outcomes of seriously ill, hospitalized adult patients. The following 5 medical centers participated in data collection: Beth Israel Hospital, Boston, Mass; Duke University Medical Center, Durham, NC; MetroHealth Medical Center, Cleveland, Ohio; St Joseph's Hospital, Marshfield, Wis; and University of California Medical Center, Los Angeles. The study was coordinated through George Washington University, Washington, DC. The statistical center was at Duke University.

SUPPORT subjects included all patients meeting severity and other entry criteria,[14] which were designed to identify patients with an aggregate 6-month mortality of 50%, in 1 or more of 9 disease categories on admission to the hospital or during an ICU stay. The disease categories were acute respiratory failure (ARF), chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), cirrhosis, nontraumatic coma, colon cancer metastatic to the liver, non–small cell cancer of the lung (stage III or IV), and multiorgan system failure (MOSF) with malignancy or sepsis. Exclusion criteria included age less than 18 years, death or discharge within 48 hours, inability to speak English, acute psychiatric disorders, pregnancy, acquired immunodeficiency syndrome (AIDS), acute burns, and head trauma or other trauma (unless acute respiratory failure or MOSF developed later). All patients were followed up for 6 months. The detailed methods for this project have been published previously.[14] We briefly describe study procedures relevant to this analysis.

Study Population

SUPPORT had 2 phases. Phase 1 was a prospective observational study designed to describe the process of decision making and the care of seriously ill patients. Phase 2 was a cluster RCT of an intervention to improve decision making and outcomes of seriously ill patients. The phase 2 intervention included delivery of information on prognosis and patient preferences to the physician and encouraging communication among patients, surrogates, and physicians.[15] For the purpose of the current analysis, data collection was identical in the 2 phases. During phase I (June 1989 to June 1991), 4301 patients were enrolled; 4804 patients were enrolled in phase II (January 1992 to January 1994). Since the intervention did not change decision making or physician behavior,[15] we combined the phase I and phase II data sets. In this analysis, we include all 5735 SUPPORT patients who were admitted to or transferred to an ICU in the first 24 hours after entering the study.

Right Heart Catheterization

The use of RHC was detected by abstraction of charts and bedside flow sheets in the ICU by specially trained nurses. Right heart catheterization was coded as present if performed within the first 24 hours after study entry (2184 patients).

Chart Abstraction

Nurse abstractors in each hospital screened all admissions the morning after admission and all ICU patients on a daily basis to identify patients meeting entry criteria. When a patient met study entry criteria, detailed chart abstraction was performed. Study protocol specified diagnostic and severity criteria for each disease category.[14] Up to 4 admission diagnoses were recorded.[16] Comorbid conditions were documented using previously validated criteria.[16] Duration of hospital stay prior to study entry was determined. Physiological status and intensity of care were assessed on days 1, 3, 7, 14, and 25 of the hospital stay. Physiological status was assessed by recording the most abnormal value in the 24-hour period for the following values: temperature, mean blood pressure, heart rate, respiratory rate, partial pressure of arterial oxygen ($Pa{O_2}$), fraction of inspired oxygen ($F{IO_2}$), partial pressure of arterial carbon dioxide ($Pa{CO_2}$), pH, sodium, potassium, hematocrit, white blood cell (WBC) count, albumin, bilirubin, creatinine, and Glasgow Coma Score. Missing measurements were assumed to have normal values.[17] The Acute Physiology and Chronic Health Evaluation (APACHE) III score was calculated.[16] An estimate of 2-month prognosis was determined using a statistical model developed for SUPPORT.[17] Intensity of care was assessed using the Therapeutic Intervention Scoring System (TISS), with all TISS points directly associated with RHC removed.[18,19]

Interviews

Patients and their designated surrogate decision makers were interviewed by trained interviewers on day 3 (window from day 2 to 6). At this interview, age, sex, race, education, income, and insurance status were elicited from the patient. If the patient was unconscious, intubated, or cognitively impaired, the surrogate interview was the source of this information. If neither interview could be performed, the information was obtained from the chart. Functional status was determined using a modified Katz Activities of Daily Living Scale (ADL)[20] and the Duke Activity Status Index (DASI).[21] When patient reports were unavailable, surrogate reports were calibrated using regression analysis and substituted for patients' responses (52%).[15] The surrogate was identified by the patient as the person who would make decisions if the patient could not. For patients without data from either source (23%), ADL and DASI were imputed based on multivariable regression models containing diagnoses, age, comorbid illness, Glasgow Coma Score, Acute Physiology Score, and site.[15]

Outcomes

The outcomes of interest for this analysis were patient survival time, hospital and ICU length of stay, hospital costs, and intensity of care. Date of death or survival to day 180 was confirmed for all patients. The hospital and ICU length of stay were determined. Total hospital charges were determined from the final hospital bill, converted to estimated costs using each hospital's ratio of costs to charges, and expressed in 1993 dollars. Since some patients had been in the hospital prior to entering the study, total estimated costs included costs incurred prior to entering the study. To estimate the costs incurred during the study period, the subpopulation of patients who entered the study on the day of admission to the hospital was used to determine the relationship between log total cost and the log of the product of the average TISS and the study length of stay stratified by site (R^2=0.88). This relationship was then used to estimate costs during the study period in all patients. Intensity of care was determined on study days 1, 3, 7, 14, and 25 using TISS with TISS points for RHC removed.

Data Quality

Chart abstractor and interviewer supervisors were trained centrally, and all sites had quarterly site visits to assure compliance with study protocol. Ten percent of all charts were randomly selected for reabstraction by a second abstractor. Overall reliability (defined as complete agreement between the 2 abstractors) was 89% for Acute Physiology Score and 86% for TISS. Seventy-five charts of ICU patients were selected randomly to check the reliability of coding the occurrence of RHC. The initial abstractors identified 32 patients with RHC and 43 patients without RHC. In all 75 cases, the second abstractor agreed with the first. The interviewer supervisor audited a 10% sample of all interviews. All interviews were checked in the field for errors and rechecked by the supervisor before data entry. Overall, 81% of eligible patients were interviewed. Patients who were unconscious, intubated, aphasic, or demented were ineligible for interviews. The response rates for surrogates and physicians were 81% and 87%, respectively. All data were double-entered at the sites and sent to the National Coordinating Center by modem. Range checks and checks for internal consistency were performed on the merged data set, and all questionable values were referred to the site to be compared with the values on the original data collection form. Over 99% of all required chart abstraction was completed according to protocol.

Propensity Score

Before any analysis, a panel of 7 specialists in critical care (4 intensivists and 3 cardiologists) specified the variables that would relate significantly to the decision to use or not to use a right heart catheter. These variables were then included in a multivariable logistic regression analysis[22] (LOGIST procedure, SAS Institute Inc, Cary, NC), with RHC in the initial 24 hours as the dependent variable. The independent variables were age, sex, race (black, white, other), years of education, income, type of medical insurance (private, Medicare, Medicaid, private and Medicare, Medicare and Medicaid, or none), primary disease category, secondary disease category, 12 categories of admission diagnosis, ADL and DASI 2 weeks before admission, do-not-resuscitate status on day 1, cancer (none, localized, metastatic), SUPPORT model estimate of the probability of surviving 2 months,[17] acute physiology component of the APACHE III score,[16] Glasgow Coma Score, weight, temperature, mean blood pressure, respiratory rate, heart rate, PaO_2/FIO_2 ratio, $PaCO_2$, pH, WBC count, hematocrit, sodium, potassium, creatinine, bilirubin, albumin, urine output, and 13 categories of comorbid illness. The logistic regression analysis was used to determine probability of RHC (from 0 to 1), the propensity score, for each patient in the data set.[12,13] Since the purpose and utility of the propensity score were to represent, as completely as possible, the relationship between multiple covariates and the use of RHC specifically for the 5735 patients in this population, external validation was not appropriate.[12,13] The adequacy of the propensity score in adjusting for the effect of the major covariates was demonstrated by testing for differences in individual covariates between patients with and without RHC after stratifying by quintiles of propensity for RHC.

Case-Matching Procedure

Patients managed without RHC were matched to patients who had RHC on the basis of disease category and the propensity score. First, a patient was randomly selected from the 2184 patients with RHC, then all 3551 patients managed without RHC were searched to find the patient with the same disease category who had the closest propensity score (within 0.03 on a scale of 0 to 1). This procedure was continued until all possible pairs were identified. Finally, the difference in propensity score within each pair was calculated, and each pair with a positive difference was matched with the pair with the negative difference closest in magnitude, assuring equal numbers of pairs with positive and negative differences in propensity.

Sensitivity Analysis

The validity of our findings depends on the propensity score providing adequate adjustment for all factors that influence the use of RHC. Since, by using the procedure described, we adjust adequately for all factors included in the propensity regression, the main risk is that there could be an important but unmeasured covariate that is not accounted for in the propensity regression. We tested the sensitivity of our analysis to a missing covariate in 3 ways. First, we asked 13 practicing clinicians who were not associated with the study to review an extensive list of potential covariates, to indicate all variables that might influence their decision to perform RHC, and to identify the 10 variables that have the greatest influence on that decision. The 10 variables chosen by all 13 clinicians were represented in the propensity score. Second, we identified the 4 variables that were most highly associated with the decision to use RHC and removed them from the propensity regression 1 at a time and in groups to determine the stability of the adjustment despite inducing an artificially inadequate model. Finally, we performed a sensitivity analysis using the method described by Rosenbaum and Rubin[23] to determine how substantial the effect of a missing (unknown) covariate would have to be to mask a true relative hazard of death of 1.0 or to hide a beneficial effect of RHC (relative hazard of 0.80).

Analysis

All analyses were performed using SAS software (SAS Institute Inc, Cary, NC). Mean (25th, 50th [median], 75th percentiles) data were used to describe continuous values. Differences between groups with and without RHC were determined by the Wilcoxon rank sum test for continuous and ordinal variables, and χ^2 test for categorical variables. Differences between the matched pairs were evaluated using the signed rank test. Differences in 30-day, 60-day, 180-day, and hospital survival were evaluated using the McNemar test. The survival curves were compared using the log rank test. The association of RHC with survival time and length of stay (after adjustment for propensity alone and after simultaneous adjustment for propensity plus age, sex, number of comorbid illnesses, ADL and DASI 2 weeks prior to admission, 2-month prognosis, day 1 Acute Physiology Score, Glasgow Coma Score, and disease category) was determined using Cox proportional hazards model[24] (PHREG procedure, SAS Institute Inc). The association of RHC with estimated hospital costs and average TISS score after adjustment, as described, was determined using linear regression[25,26] (REG procedure, SAS In-

Table 1.—Characteristics of 5735 Critically Ill Patients*

Variable	No RHC (n=3551)	RHC (n=2184)
Age range, y†		
<50	884 (25)	540 (25)
50 to <60	546 (16)	371 (17)
60 to <70	812 (23)	577 (26)
70 to <80	809 (23)	529 (24)
>80	500 (14)	167 (8)
Sex†		
Male	1914 (54)	1218 (59)
Female	1637 (46)	906 (41)
Race		
White	2753 (78)	1707 (78)
Black	585 (17)	335 (15)
Other	213 (5)	142 (7)
Disease category†		
ARF	1200 (34)	589 (27)
MOSF	1245 (35)	1235 (57)
CHF	247 (7)	209 (10)
Other	859 (24)	151 (7)
Cancer†		
None	2652 (75)	1727 (79)
Localized	638 (18)	334 (15)
Metastatic	261 (7)	123 (6)
DNR status, day 1†		
Yes	710 (20)	296 (14)
APACHE III score (without Glasgow Coma Score)†	51 [38, 50, 62]	61 [47, 60, 74]
Probability of 2-mo survival		
Model estimate†	0.61 [0.49, 0.65, 0.76]	0.56 [0.45, 0.60, 0.72]
Physician estimate†	0.51 [0.10, 0.50, 0.80]	0.41 [0.05, 0.50, 0.75]
No. of comorbid illnesses†	1.7 [1, 2, 3]	1.6 [1, 1, 2]
ADLs 2 wk prior	1.6 [0.5, 1.1, 2.4]	1.5 [0.5, 1.1, 2.2]
DASI 2 wk prior†	20 [16, 20, 23]	21 [17, 20, 23]
LOS prior to study entry, d†	4.6 [0, 0, 5]	6.4 [0, 2, 8]
Temperature, °C	37.6 [36.2, 38.1, 39.0]	37.6 [36.1, 38.1, 39.0]
Heart rate, beats/min†	112 [76, 120, 140]	119 [105, 125, 145]
Blood pressure, mm Hg†	85 [53, 68, 119]	68 [47, 57, 73]
Respiratory rate, breaths/min†	29 [20, 30, 39]	27 [12, 28, 37]
WBC count $\times 10^9$L†	15.2 [8.2, 13.6, 19.4]	16.2 [8.6, 14.7, 21.2]
Pa_{O_2}/F_{IO_2}, mm Hg†	240 [149, 224, 333]	192 [110, 168, 267]
Pa_{CO_2}, mm Hg†	40 [32, 38, 44]	37 [30, 36, 40]
pH†	7.39 [7.35, 7.40, 7.46]	7.38 [7.32, 7.40, 7.46]
Creatinine, µmol/L (mg/dL)†	168 (1.9) [80, 115, 177] (0.9, 1.3, 2.0)	221 (2.5) [106, 159, 265] (1.2, 1.8, 3.0)
Albumin, g/L†	32 [27, 35, 35]	29 [24, 35, 35]
Glasgow Coma Score†	11 [7, 14, 15]	10 [4, 13, 15]

*Data presented as No. (%) or mean [25th, 50th (median), and 75th percentiles]. RHC indicates right heart catheterization; ARF, acute respiratory failure; MOSF, multiorgan system failure; CHF, congestive heart failure; DNR, do not resuscitate; APACHE, Acute Physiology and Chronic Health Evaluation; ADLs, activities of daily living; DASI, Duke Activity Status Index; LOS, length of stay; WBC, white blood cell; Pa_{O_2}, partial pressure of arterial oxygen; F_{IO_2}, fraction of inspired oxygen; and Pa_{CO_2}, partial pressure of arterial carbon dioxide.
†$P \leq .001$.

stitute Inc). Subgroup analysis was performed using Cox proportional hazards model to determine the association of RHC with survival time at the 5 study sites and in prespecified patient subgroups. Correction for multiple comparisons[27] was used when analyzing for differences between RHC and no RHC among multiple covariates stratified by propensity.

RESULTS

Description of the Study Population

Of the 9105 SUPPORT patients, 5735 (63%) received care in an ICU during the first day of enrollment in SUPPORT. Right heart catheterization was performed in 2184 patients (38%) within the initial 24 hours of the ICU stay. An additional 308 patients (5%) received RHC by 72 hours. For the analyses that follow, the 2184 patients managed with RHC in the first 24 hours are compared with the 3551 managed without RHC.

Patient and Disease Characteristics

The characteristics of the 5735 patients are shown in Table 1. Patients managed with RHC were more likely to be male, to have private insurance, and to enter the study with ARF, MOSF, or CHF. Patients with RHC were less likely to be over the age of 80 years, to have cancer, or to have a do-not-resuscitate order in the first 24 hours of hospitalization. All patients in the study were quite ill, but patients with RHC had significantly higher APACHE III Acute Physiology Scores and a lower probability of 2-month survival as estimated by their physicians and by an estimate calculated using the SUPPORT prognostic model[17] (Table 1). They had fewer comorbid conditions and tended to have been hospitalized longer before entering the study. The values for vital signs, WBC count, arterial blood gases, serum creatinine, serum albumin, and Glasgow Coma Score were more abnormal in patients with RHC.

Unadjusted Outcomes

Patients with RHC had significantly lower 30-, 60-, and 180-day survival than patients managed without RHC (Table 2). Total hospital costs after study entry also were significantly higher in patients with RHC. Patients with RHC were in the ICU and in the hospital longer than patients without RHC.

Propensity Score

The multivariable regression of propensity for RHC had an area under the receiver operating characteristics curve of 0.83, indicating good discrimination between patients managed with and without RHC. There was considerable overlap in the propensity scores of patients with and without RHC. Patients managed with RHC had a mean propensity score of 0.577 (95% confidence interval [CI], 0.108-0.943), while those

Table 2.—Unadjusted Relationship of Right Heart Catheterization (RHC) to Outcomes for 5735 Critically Ill Patients*

Outcome	No RHC (n=3551)	RHC (n=2184)	P
Survival, No. (%)			
30 d	2463 (69.4)	1354 (62.0)	<.001
2 mo	2231 (62.8)	1190 (54.5)	<.001
6 mo	1906 (53.7)	1012 (46.3)	.001
Resource utilization†			
Total costs (× $1000)‡	74.3 [18.4, 37.1, 81.5]	131.9 [42.1, 81.7, 160.6]	<.001
Average TISS	28 [21, 27, 35]	35 [28, 35, 42]	<.001
Length of stay, d†			
ICU	10.3 [3, 6, 11]	15.5 [5, 9, 18]	<.001
Study	20.5 [8, 13, 23]	25.7 [9, 17, 32]	<.001

*TISS indicates Therapeutic Intervention Scoring System (with points associated with RHC removed); and ICU, intensive care unit.
†Continuous variables are presented as mean [25th, 50th (median), and 75th percentiles].
‡Total costs are estimated hospital costs from study day 1 to discharge (see "Methods" for details).

managed without RHC had a mean propensity score of 0.253 (95% CI, 0.011-0.779). The ability of the propensity score to adjust for important covariates of RHC was evaluated by testing for differences in these covariates within quintiles of propensity. The values for important variables associated with the use of RHC including severity of illness, mean blood pressure, heart rate, respiratory rate, pH, PaO_2/FIO_2, $PaCO_2$, disease category, and prognosis were not significantly different for patients managed with and without RHC when compared within quintiles of propensity for RHC (Figure 1).

Adjustment for Treatment Selection Bias: Case Matching (n=2016)

There were 2016 patients in 1008 pairs managed with and without RHC who were successfully matched for disease category and propensity for RHC (Table 3). The disease categories were as follows: ARF in 46%, MOSF in 34%, CHF in 11%, and other diseases (COPD, cirrhosis, nontraumatic coma, and lung cancer) in 10%. In paired analyses, there were no differences detected in these 2016 patients between those managed with and those managed without RHC for 18 variables including severity of illness, 2-month prognosis on day 1, age, number of comorbid illnesses, functional status, vital signs, Glasgow Coma Score, WBC count, blood gases, creatinine, or albumin (Table 3).

For matched pairs, survival of patients managed with RHC was consistently lower when examined 30, 60, and 180 days after study entry (Table 4). The odds ratio (OR) was 1.24 to 1.27 for these 3 survival intervals, indicating higher odds of death in patients managed with RHC. Patients managed with RHC also had lower hospital survival, with an OR of 1.39. The 30-day survival curve for 1008 patient pairs managed with and without RHC is shown in Figure 2. For each of the 30 days after study entry, the 1008 patients managed with RHC had lower survival than the 1008 managed without RHC (P=.02). Patients managed with RHC had higher cost of hospital care, higher intensity of care, and a longer stay in the ICU than a matched population of patients managed without RHC (Table 5).

Adjustment for Treatment Selection Bias: Multivariable Analysis (n=5735)

After adjustment using propensity for RHC as well as additional adjustment for age, sex, comorbid illness, disease category, severity of illness, Glasgow Coma Score, 2-month prognosis on day 1, ADL, and DASI, the overall relative hazard of death by 30 days for patients managed with RHC was 1.21 (95% CI, 1.09-1.25; P<.001) (Figure 3). After the same adjustment, the relative hazard of death for patients with ARF was 1.30 (95% CI, 1.05-1.61; P<.001), for patients with MOSF was 1.32 (95% CI, 1.11-1.57; P<.001), and for patients with CHF was 1.02 (95% CI, 0.55-1.89; P=.94). For all patients not in the ARF, MOSF, or CHF categories (designated "all others") the relative hazard was 1.06 (95% CI, 0.80-1.41; P=.67). This group consisted of patients with severe COPD (414; 10.9% with RHC), severe cirrhosis (198; 17.7% with RHC), nontraumatic coma (359; 18.1% with RHC), non–small cell lung cancer (35; 14.7% with RHC), and colon cancer with liver metastases (5; 20% with RHC). To determine whether or not RHC later in the hospital stay was associated with better outcomes, we developed a propensity score (receiver operating characteristics area, 0.84) for RHC by 72 hours in the 3551 patients managed without RHC on day 1. The adjusted relative risk of death associated with RHC on day 3 was 1.12 (95% CI, 0.91-1.36).

The independent association of RHC with utilization of resources was also assessed. After multivariable adjustment as described, management with RHC was associated with significantly higher mean±SE total hospital costs ($7900±$3900; P<.001). Patients with RHC also had a greater mean±SE intensity of care, indicated by higher mean±SE TISS scores (7.0±0.3 points; P<.001, with RHC-associated points removed) and longer stay in the ICU (2.2±0.5 days; P<.001). The adjusted hospital LOS after study entry was not significantly different between the 2 groups (1.5±0.8 days; P=.07).

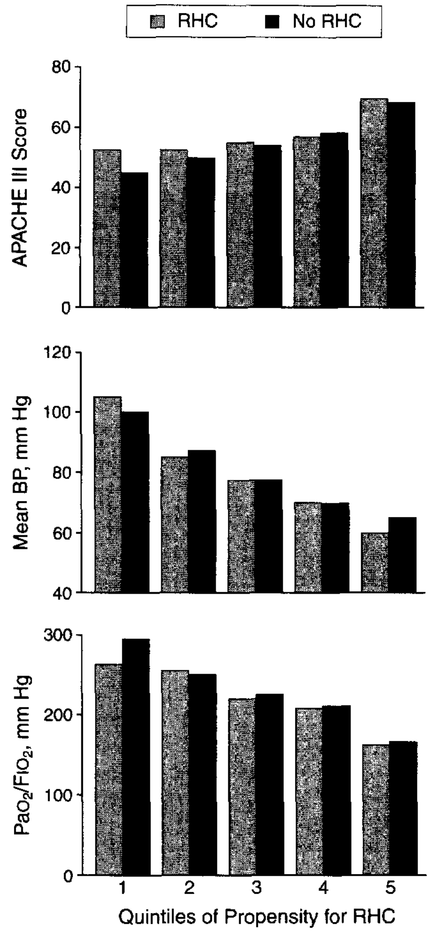

Figure 1.—Stratification by the propensity score minimizes treatment selection bias. Patients were stratified into 5 equal quintiles using the propensity score. Within each quintile, patients managed with right heart catheterization were compared with patients managed without right heart catheterization for each of the variables shown. There was no difference in Acute Physiology and Chronic Health Evaluation (APACHE) III Acute Physiology Score, mean blood pressure, or partial pressure of arterial oxygen/fraction of inspired oxygen (PaO_2/FIO_2) between the 2 groups within any of the quintiles. RHC indicates right heart catheterization.

Table 3.—Characteristics of 1008 Matched Pairs of Patients Managed With and Without Right Heart Catheterization (RHC)*

Variable	No RHC (n=1008)	RHC Day 1 (n=1008)	P
Propensity for RHC	0.51 [0.35, 0.50, 0.67]	0.51 [0.36, 0.50, 0.67]	.85
Acute Physiology Score (without Glasgow Coma Score)	57 [44, 58, 71]	57 [43, 57, 70]	.34
Model estimate, probability of 2-mo survival	0.58 [0.46, 0.62, 0.74]	0.59 [0.47, 0.62, 0.74]	.43
Age, y	60 [49, 63, 72]	60 [49, 62, 73]	.97
No. of comorbid illnesses	1.6 [1, 1, 2]	1.6 [1, 1, 2]	.40
ADLs 2 wk prior	1.5 [0, 1, 2]	1.5 [0, 2, 2]	.43
DASI 2 wk prior	21 [16, 20, 24]	21 [17, 20, 24]	.48
LOS prior to study entry, d	6.8 [0, 2, 8]	6.5 [0, 2, 8]	.46
Temperature, °C	37.7 [36.1, 38.3, 39.1]	37.7 [36.2, 38.2, 39.0]	.92
Heart rate, beats/min	111 [105, 125, 145]	111 [103, 124, 145]	.75
Blood pressure, mm HG	73 [49, 61, 108]	71 [49, 60, 81]	.60
Respiratory rate, breaths/min	28 [19, 30, 38]	28 [14, 28, 38]	.30
WBC count × 10^9L	15.3 [8.2, 14.0, 20.0]	15.0 [7.4, 13.6, 20.0]	.53
Pao_2/Fio_2, mm Hg	210 [127, 185.7, 296]	211 [120, 192, 305]	.70
$Paco_2$, mm Hg	37 [31, 36, 41]	38 [31, 36, 40]	.80
pH	7.39 [7.34, 7.40, 7.46]	7.39 [7.34, 7.40, 7.46]	.74
Creatinine, µmol/L (mg/dL)	203 (2.3) [88, 141, 230] (0.1, 1.6, 2.6)	203 (2.3) [106, 150, 239] (1.2, 1.7, 2.7)	.38
Albumin, g/L	30 [25, 35, 35]	30 [26, 35, 35]	.77
Glasgow Coma Score	13 [12, 15, 15]	13 [12, 15, 15]	.35

*Continuous variables are presented as mean [25th, 50th (median), 75th percentiles]. See Table 1 for explanation of abbreviations.

Table 4.—Relationship of Right Heart Catheterization (RHC) to Survival for Matched Pairs of Patients Managed With and Without RHC*

	Survival, No. (%)			
Survival Interval	No RHC (n=1008)	RHC (n=1008)	OR (95% CI)	P
30 d	677 (67.2)	630 (62.5)	1.24 (1.03-1.49)	.03
60 d	604 (59.9)	550 (54.6)	1.26 (1.05-1.52)	.01
180 d	522 (51.2)	464 (46.0)	1.27 (1.06-1.52)	.009
Hospital	629 (63.4)	565 (56.1)	1.39 (1.15-1.67)	.001

*OR indicates odds ratio; and CI, confidence interval.

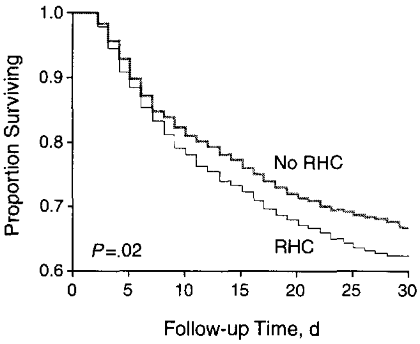

Figure 2.—Thirty-day survival curves for 2016 patients with and without right heart catheterization (RHC) matched for disease category and propensity score (case-matched analysis). Proportion of patients surviving with RHC and without RHC are shown over the 30 days after study entry. Survival is significantly better in the population managed without RHC.

Analysis by Subgroup and by Prognosis

Analysis of prespecified patient subgroups revealed that the adjusted relative hazard of death by 30 days with RHC tended to be higher in elderly patients, women, whites, patients with shock or sepsis, and patients receiving postoperative care (Figure 4). The relative hazard was greater than 1 at each of the 5 sites, and there were no significant differences among the sites. There was no single subset of patients for whom the relative hazard of death was significantly reduced by using RHC. Figure 5 shows the relationship between the relative hazard of death by 30 days and the 2-month prognosis at study entry (estimated probability of being alive at 2 months). Patients with a predicted probability of 2-month survival on study entry greater than 0.60 tended to have increased risk of death by 30 days when RHC was used.

Sensitivity Analysis

We performed several analyses to assess the sensitivity of the adjustment for treatment selection bias to the effect of missing variables. First, 13 practicing clinicians were asked to indicate the 10 variables with the greatest influence on their decision to use RHC. All chosen variables were represented in the propensity score. Second, we determined how sensitive the model was to the removal of the physiological variables with the largest independent effect on the probability of RHC in the propensity regression (Pao_2/Fio_2, mean blood pressure, heart rate, and respiratory rate). The relative hazard of death changed only 0.01 when any single variable was removed. Finally, we performed a sensitivity analysis[23] designed to estimate the effect of a possible missing (or unknown) variable on adjustment using the propensity score. We determined that the covariate missing from the propensity score would have to increase the risk of death 6-fold and increase the probability of RHC 6-fold for a true relative hazard of 0.80 to be misrepresented as a relative hazard of 1.21. In addition, a true relative hazard of 1.0 could be misrepresented as 1.21 if a missing covariate that simultaneously increased the risk of death 3-fold and the probability of RHC 3-fold was not accounted for in the propensity score.

COMMENT

We evaluated the association of RHC with patient outcomes after adjusting for a wide range of potentially confounding variables using 2 different analytic procedures. First, we identified 1008 pairs of patients managed with and without RHC who were matched for disease category and propensity for RHC. As expected,[12,13] this procedure resulted in even distribution of risk factors between the treatment groups. Once controlling for disease and propensity score, the patients managed with RHC were not different from matched patients managed without RHC when compared for a variety of demographic and physiological characteristics. However, in these 2 populations of patients with the same patient characteristics and the same probability of catheterization, patients managed with RHC had higher mortality, greater intensity of care, and longer stays in the ICU.

Second, we used multivariable analysis to evaluate the association of RHC with patient outcomes within the entire population of 5735 patients. As was seen with the case-matched analysis, after adjustment for treatment selection bias using the propensity score, RHC was associated with an increased risk of death. Analysis of important clinical subgroups did not reveal a group in which RHC was associated with increased survival time. Again, management of critically ill patients with RHC was associated with more intense care, longer stays in the ICU, and higher hospital costs.

The results of analyses of survival time within disease groups, in predefined subgroups, and across levels of severity of illness are also compatible with either a neutral or detrimental effect of RHC. The relative hazard of death was greater than 1 for acute respiratory failure and MOSF, 2 common indications for RHC. Patients with CHF demonstrated a relative hazard of 1. Right heart catheterization was associated with the highest risk in postoperative patients and in the least severely ill patients.

There are several possible explanations for these results. First, RHC may lead directly to worse patient outcomes, presumably because the deleterious effects of RHC outweigh the benefits of the procedure. Clearly, complications of RHC such as line sepsis,[28,29] bacterial endocarditis,[30] and large vein thrombosis[30,31] may increase mortality, prolong hospital stay, and increase costs.[32-35] In addition, the benefits of RHC may not be realized if the physician interpreting the output of the catheter is not knowledgeable and skilled in its use.[36]

Another possible explanation for our findings is that RHC is a marker for an aggressive or invasive style of care that may be responsible for a higher mortality rate and higher costs. This would be consistent with the findings of Blumberg and Binns[10] in patients with acute myocardial infarction. In their study, hospitals with the higher than predicted use of RHC had higher than expected mortality rates. We found that patients with RHC had higher TISS scores than patients without RHC, despite the fact that all TISS points associated with RHC had been removed. A point may be reached in the care of some critically ill patients where adding another procedure provides little marginal benefit to the patient while exposing them to all the risks of the procedure. In this setting, a less invasive approach may be associated with better outcomes.

A third possibility is that change in therapy in response to the information provided by RHC may lead to higher mortality. There is controversy at present about the role of fluid resuscitation[37,38] and the aggressive use of inotropic agents in the care of lung injury and MOSF.[39,40] Right heart catheterization is necessary to guide fluid and inotropic therapy to achieve "supranormal values" of cardiac output and oxygen delivery in patients with MOSF.[39,40] However, an initial RCT of this approach in critically ill patients reported a 67% higher mortality rate,[41] and a subsequent larger trial confirmed a lack of benefit.[42] If a substantial number of physicians in our study hospitals followed the practice of aggressive use of fluids and inotropic agents to achieve "supranormal" values of cardiac output, this practice might have contributed to a lack of benefit from RHC.

A fourth possible explanation is that RHC is actually beneficial and that we missed this relationship because we did not adequately adjust for some confounding variable that increased both the likelihood of RHC and the likelihood of death. As we found in this study, RHC is more likely to be used in sicker patients who are also more likely to die. We used a propensity score[12,13,43-45] to adjust for a wide variety of demographic, clinical, and physiological factors that relate to the decision to use RHC. We also performed analyses to assess how strong a missing (or unknown) covariate would have to be to significantly affect the results of this study. First, we determined that a missing variable with an independent effect equal to the strongest variables in the propensity regression would not change

Table 5.—Relationship of Right Heart Catheterization (RHC) to Resource Use for Matched Pairs of Patients Managed With and Without RHC*

	No RHC (n=1008)	RHC (n=1008)	P
Resource utilization			
Total costs (× $1000)†	35.7 (11.3, 20.6, 39.2)	49.3 (17.0, 30.5, 56.6)	<.001
Average TISS (adjusted)	30 (23, 29, 38)	34 (27, 34, 41)	<.001
Length of stay, d			
ICU	13.0 (4, 7, 14)	14.8 (5, 9, 17)	<.001
Study	23.8 (9, 15, 28)	25.1 (9, 16, 31)	.14

*Continuous variables are presented as mean (25th, 50th [median], 75th percentiles). TISS indicates Therapeutic Intervention Scoring System (with points associated with RHC removed); and ICU, intensive care unit.

†Total costs are estimated hospital costs from study day 1 to discharge (see "Methods" for details).

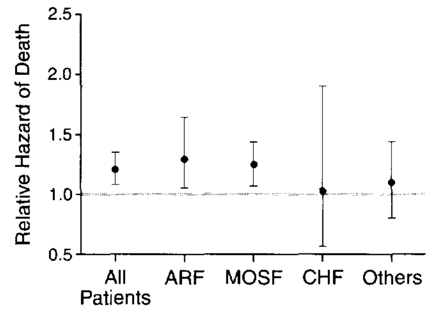

Figure 3.—Association of right heart catheterization with survival time, overall and within disease categories. The relative hazard of death associated with right heart catheterization after adjustment for treatment selection bias is shown for all 5735 intensive care unit (ICU) patients as well as for patients with acute respiratory failure (ARF; n=1789), multiorgan system failure (MOSF; n=2480), congestive heart failure (CHF; n=456), and the 1010 other ICU patients (see text for description). Error bars represent the 95% confidence intervals for the relative hazard of death.

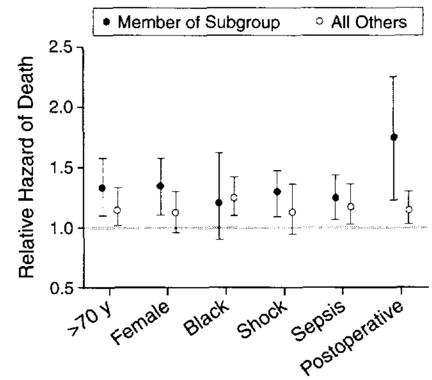

Figure 4.—Association of right heart catheterization with survival time in important subgroups. The adjusted relative hazard of death is shown for 6 clinical subgroups. Patients in each subgroup are shown in solid circles while all other patients (those not meeting subgroup criteria) are shown in the open circles. The subgroup criteria are (1) age greater than 70 years; (2) female sex; (3) African-American descent (designated "Black" for brevity); (4) shock (mean blood pressure <60 mm Hg); (5) sepsis (SUPPORT criteria); and (6) postoperative (met SUPPORT entry criteria after a major operative procedure). Error bars represent the 95% confidence intervals for the relative hazard of death.

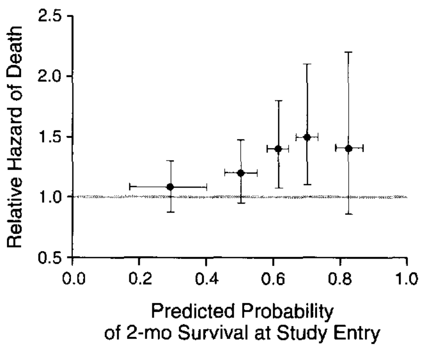

Figure 5.—Relationship between prognosis at study entry and relative hazard of death associated with right heart catheterization. All 5735 intensive care unit (ICU) patients were stratified into 5 equal groups on the basis of prognosis at study entry (predicted probability of being alive at 2 months).[17] Adjusted relative hazard of death over 30 days was determined and is shown with 95% confidence intervals within each group. The relative hazard of death was highest in patients with greater than 0.60 predicted probability of surviving 2 months and was lowest in the group with the worst 2 month prognosis.

our results. Second, the sensitivity analysis[23] demonstrated that a missing covariate would have to increase both the likelihood of RHC and the likelihood of death 6-fold to mask a significant beneficial effect of RHC. The effect of this missing variable would have to be independent of the variables already in the propensity score and not recognized or reported by experienced clinicians. None of the variables in the propensity score had such a strong effect.

Gore et al[7] were among the first to report an increased relative risk of death both overall and in subgroups of patients whose myocardial infarction was complicated by CHF, hypotension, and shock. This increased risk of death persisted after adjustment for age, sex, peak creatine phosphokinase, and the occurrence of a Q-wave infarct. Greenland et al,[9] in another observational study of 5841 patients with acute myocardial infarction, reported that the RHC had an OR of death of 1.66 (95% CI, 1.05-2.62) in women and 3.88 (95% CI, 2.85-5.30) in men after adjustment for age, CHF, hypotension, atrioventricular block, diabetes mellitus, history of and location of myocardial infarction, and elevated lactate dehydrogenase. Blumberg and Binns[10] reported increased mortality rates in elderly patients with new myocardial infarction cared for in hospitals with a higher than expected rate of RHC. Wu et al[6] reported that use of RHC was an independent predictor of hospital mortality.

The costs of catheterization and subsequent manipulation, measurements, and care associated with RHC are estimated to be $2000 per patient.[46] Tuman et al[47] compared the use of RHC vs central venous catheterization for monitoring patients during and after coronary artery bypass surgery. They found longer ICU stays and higher use of vasoactive and inotropic infusions in patients managed with RHC. Our findings confirm the presence of substantially higher costs with RHC but suggest that a large part of the cost is attributable to the tendency of RHC to be associated with the use of other expensive technology and with increased nursing care. Patients with RHC spent 2 days longer in the ICU and the average intensity of care was 4 to 7 TISS points higher. The longer length of stay and the higher average intensity of care led to substantially higher costs per hospital stay.

Limitations

There are several important limitations of this study. First, it is an observational study, not an RCT. While we have adjusted for treatment selection bias more extensively than any prior study of this procedure and have determined that an important missing covariate that would change the results is unlikely, the possibility of an important missing covariate can never be entirely excluded. Second, this study represents practice in only 15 ICUs and 5 tertiary care hospitals. These hospitals may treat a population with more complex illnesses in whom a beneficial effect of RHC may have been more difficult to detect. Third, we report only the association between use of RHC in the first 24 hours of an ICU stay and specific patient outcomes. Right heart catheterization used later in the hospital stay may be more beneficial. However, it is important to note that 81% of all RHCs we identified were performed in the first 24 hours and that 93% were inserted by 72 hours.

Our findings run counter to published recommendations for the use of RHC[48-51] and to the broad clinical application of this procedure.[52] Thus, it is important to weigh the findings of this study carefully. We present evidence that RHC may not benefit critically ill patients and may even be harmful. However, evidence is not the same as proof. Some will argue that, since we have shown that RHC may be harmful, its use should be severely restricted. Others will ignore our findings since our study was observational in design and they believe that only an RCT can provide accurate information about the risk or benefit of a procedure. From our perspective, the best approach lies somewhere between these 2 points of view.

This study raises serious concerns about the role of RHC in the care of the critically ill. These concerns ought to be addressed promptly. Our findings should be confirmed using data from other observational studies. The mechanisms by which RHC may harm patients should be explored. Finally, we hope that the findings from this study may create an environment in which an RCT can be performed. The strongly held clinical assumption that RHC improves patient outcomes was the major reason that a recent attempt at an RCT was aborted.[5] This analysis may create sufficient uncertainty about the benefit of this procedure that an RCT can be ethically performed.

Conclusion

In this observational study, RHC was associated with an increased risk of mortality and increased resource use despite adjustment for treatment selection bias and for a variety of risk factors related to survival and resource use. The results persisted after examining multiple subgroups and varying levels of severity of illness. This study raises important questions regarding the incremental value of RHC in the treatment of a variety of ICU patients.

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