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# The Pulmonary Artery Catheter in Anesthesia Practice in 2007: An Historical Overview With Emphasis on the Past 6 Years

Andrew B. Leibowitz, MD, and John M. Oropello, MD

The pulmonary artery catheter has been widely used in anesthesiology and critical care medicine. Until recently, only retrospective or relatively weak prospective studies examining its effect on outcome had been performed. Over the past 6 years, however, a number of well-designed prospective trials and statistically sound retrospective studies have been completed. All of these show no benefit and some even reveal a potential for increased morbidity. Reasons for this device's inability to improve outcome are numerous, including wrong patient selection and misinterpretation, but the most impressive and convincing evidence is that filling pressures measured

from the catheter, particularly the pulmonary artery "wedge" pressure, have no physiologic value. The wedge pressure has been shown to not correlate with other accepted methods of determining left ventricular filling or volume or intravascular volume and also does not help to generate cardiac function curves. Therefore, knowledge of it may actually lead to incorrect management more frequently than not.

**Keywords:** pulmonary artery catheter; anesthesiology; critical care; outcome; myocardial infarction; sepsis; adult respiratory distress; echocardiography

The pulmonary artery catheter (PAC) has been the mainstay of invasive hemodynamic monitoring for 35 years. Despite the tens of millions of catheters used, it is probably the most controversial invasive medical device ever introduced into clinical practice. Over the past 6 years, since the Updated Report by the American Society of Anesthesiologists Task Force on Guidelines for Pulmonary Artery Catheterization was written,<sup>1</sup> several large, statistically sound studies have been published that should directly affect the way anesthesiologists choose to use this monitor in their practice. It is the goal of this article to give a historical overview of the first 30 years of literature, to review the newer studies in greater depth, some

of which have already achieved "landmark" status, and to specifically address the utility of monitoring cardiac filling pressures.

## Historical Overview: 1970-2000

The PAC was developed by Swan, Ganz, et al<sup>2</sup> and revealed in their milestone publication in 1970. The clinical utility of the catheter was established in 1976, when a 2-part article was published demonstrating that patients with myocardial infarction and hemodynamic compromise could be managed by application of catheter derived hemodynamic subsets.<sup>3,4</sup> Within the next decade, several investigations appeared to show that use of these catheters in patients suffering from a wide variety of hemodynamic abnormalities and insults markedly improved outcomes.

Of greatest interest to anesthesiologists were the studies that purported to demonstrate that perioperative pulmonary artery catheterization, usually combined with rigorous intensive care unit (ICU) management, resulted in dramatically lower morbidity and mortality.

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**Table 1.** Randomized Controlled Trials of Pulmonary Artery Catheter (PAC) Use in Peripheral Vascular Surgery (PVD) and Abdominal Aortic Aneurysm Repair (AAA)

Author	Year	Patient Group	Total Number of Patients	PAC/No PAC	Directed Therapy	Significant Outcome Differences
Isaacson et al <sup>7</sup>	1990	AAA	102	49/53	No	None
Joyce et al <sup>8</sup>	1990	AAA	40	21/19	No	None
Berlauk et al <sup>9</sup>	1991	PVD	89	68/21	Yes	Less graft thrombosis in PAC group
Bender et al <sup>10</sup>	1997	AAA and PVD	104	51/53	Yes	None
Valentine et al <sup>11</sup>	1998	AAA	120	60/60	Yes	None
Bonazzi et al <sup>12</sup>	2002	AAA and PVD	100	50/50	Yes	None

In 1983, Rao et al<sup>5</sup> reported the incidence of recurrent perioperative myocardial infarction retrospectively during 1973-1976 and prospectively during 1977-1982.<sup>5</sup> The overall reinfarction rate dropped from 7.7% to 1.9% ( $P < .005$ ), and more specifically, when the previous infarction was 0 to 3 and 4 to 6 months old, perioperative reinfarction decreased from 36% and 26%, to 5.7% and 2.3%, respectively ( $P < .05$ ). Whether these sizable improvements in outcome were attributable to the PAC, improved intensive care, better pharmacologic management, or a combination of these factors was unclear.

Surgeons also embraced the PAC as a way to optimize patients undergoing high-risk surgery. For example, Whittemore et al<sup>6</sup> reported that in patients undergoing abdominal aortic aneurysm surgery, by using a catheter the left ventricular performance was optimized and "there were no 30-day operative deaths among the [110] patients in this series and only one in-hospital mortality (0.9%), four months following surgery. The five-year cumulative survival rate for patients in the present series was 84%, a rate which does not differ significantly from that expected for a normal age-corrected population."<sup>6(p14)</sup>

Of all perioperative indications, major vascular surgery, particularly infrarenal aortic aneurysm repair, became the most rigorously studied setting in the 1990s when several small trials were performed. All concluded that at least in a lower risk population of patients without significant renal insufficiency or congestive heart failure, use of a PAC conferred no apparent benefit<sup>7-12</sup> (see Table 1).

The only trial demonstrating an improvement in outcome from catheter use in vascular surgery was published by Berlauk et al,<sup>9</sup> who studied 3 groups of peripheral vascular surgery patients randomized to a 3-hour or a 12-hour "tune-up" based on PAC data or a group with no catheter at all. This trial was significantly flawed because there was a very high graft

thrombosis rate in the control group (4 of 21 patients) and "data were analyzed periodically for significant difference in the primary clinical outcome variable [and] when the between-group differences reached  $P < .05$  for this variable, the study was terminated."<sup>9(p219)</sup> Bender et al<sup>10</sup> used an almost identical protocol and demonstrated no improvement in outcome in the group of patients managed with a catheter.

A meta-analysis published in 2001 searched for all articles on pulmonary artery catheterization, optimization, oxygen delivery, and preoperative preparation of vascular surgery patients. It found that "of hundreds of possible papers only four were found to be adequate randomized prospective studies with similar exclusions, therapeutic endpoints, and interpretable complication and mortality rates."<sup>13(p674)</sup> In total, 174 patients were managed in a control style fashion versus 211 in a protocol group. "Power analysis showed that the combined sample sizes were adequate [and] meta-analysis indicated that in moderate-risk vascular surgery patients routine preoperative pulmonary artery catheterization is not associated with improved outcomes."<sup>13(p674)</sup>

In retrospect, it appears that earlier reports such as Whittemore's may have merely showed that aggressive preoperative hydration and attentive hemodynamic management were the cause of the improvements in outcome, not catheter use per se.

In the mid-1980s, enthusiasm for PACs was further heightened when Connors et al<sup>14</sup> showed that clinical assessment was often at odds with PAC data. Although this study only demonstrated that the 2 methods of examination led to different conclusions, not whether 1 conclusion was correct or whether the resulting different management strategy was associated with better outcome, the dye was cast in most physicians' minds; physical exam and diagnosis of critically ill patients were frequently wrong and insertion of a

catheter was the only way to tell whether the patient needed fluids, diuresis, inotropes, or vasopressors. This furthered anesthesiologists' embrace of this technology because they thought that intraoperative assessment was incorrect as frequently as the physical examinations and diagnosis shown in Connors' study and thus the catheter should be of even greater benefit to their management of high-risk and unstable perioperative patients.

Thus, by 1985, patient groups of interest to anesthesiologists who were believed to benefit from this monitor included those undergoing major vascular surgery, cardiac surgery, neurosurgery, and trauma surgery and those likely to experience major fluid shifts in the course of their perioperative care. Even age alone was believed to be an indication when 1 study suggested that elderly patients frequently had silent hemodynamic deficits that, if addressed, resulted in better outcomes.<sup>15</sup>

In 1987, these virtually unanimously positive studies were interrupted by the first report suggesting that the catheter's use may actually be harmful. Gore et al<sup>16</sup> reported that mortality from myocardial infarction was actually increased by PAC use. In fact, "the in-hospital case fatality rate for patients in CHF with a PA catheter was 44.8% compared to 25.3% for patients without a PA catheter ( $P < .001$ ). For patients with hypotension and a PA catheter, in-hospital CHF was 48.3% compared to 32.2% for hypotensive patients not receiving a PA catheter ( $P < .001$ ). . . . Use of a PA catheter was associated with an increased length of hospital stay irrespective of the development of acute clinical complications. Long-term prognosis for discharged hospital survivors who had a complicated [myocardial infarction] for up to a five-year follow-up period was similar whether the patient did or did not receive a PA catheter during the acute period of hospitalization."<sup>16(p721)</sup> The main problem with this investigation was that it was essentially a chart review, case-control study and not a randomized controlled trial and was not retrospectively risk-adjusted using multivariate analysis. Nonetheless, the accompanying editorial calling for a moratorium on PAC use resulted in heated debates over the merit of a device that was now being used in an estimated 1 million patients per year in the United States alone.<sup>17</sup>

Notably, in 2005, a similar investigation using better statistical analysis reached the same conclusions.<sup>18</sup> A retrospective study of 26 437 patients with acute coronary syndromes participating in 2 large multicenter, international randomized clinical trials revealed that "mortality at 30 days was substantially higher

among patients with PAC for both unadjusted (odds ratio 8.7; 95% confidence interval, 7.3-1.2) and adjusted analyses (odds ratio 6.4; 95% confidence interval, 5.4-7.6) in all groups except in patients with cardiogenic shock (odds ratio 0.99; 95% confidence interval, 0.80-1.23)."<sup>18(p482)</sup>

From 1987 to 1995, no large, significant investigation of the PAC was reported, and prospective trials could barely be contemplated because of the difficulties inherent in carrying out a trial of an invasive device that had already become so ingrained in everyday practice. In fact, 1 attempt to conduct a randomized controlled trial in ICU patients failed in 1991, when 33 of 148 potentially eligible patients were randomized.<sup>19</sup> The studies of patients undergoing peripheral vascular surgery and aortic reconstruction previously discussed were almost always conducted in relatively small groups of patients (ie, approximately 100), and all suffered from a variety of methodological concerns.<sup>7-12</sup>

The main academic discussion regarding pulmonary artery catheterization during this period centered on the hypothesis that critically ill patients could have improvement in outcome if their systemic oxygen delivery was deliberately raised, an idea first championed by Shoemaker et al.<sup>20</sup> Shoemaker was the founding editor of the journal *Critical Care Medicine* and one of the world's most influential intensivists.

In 1995, Hayes et al<sup>21</sup> conducted a randomized trial to determine whether infusing dobutamine (if volume expansion alone did not achieve these goals) would improve outcome using the following goals: a cardiac index greater than 4.5 L/min/m<sup>2</sup> of body surface area, oxygen delivery greater than 600 L/min/m<sup>2</sup>, and oxygen consumption greater than 170 L/min/m<sup>2</sup>. A total of 109 patients were studied. In 9 patients, the therapeutic goals were achieved with volume expansion alone; all 9 of these patients survived to leave the hospital. Fifty patients were randomly assigned to the treatment group and 50 to the control group. During treatment, there were no differences between the 2 groups in mean arterial pressure or oxygen consumption, despite a significantly higher cardiac index and level of oxygen delivery in the treatment group ( $P < .05$ ). Although the predicted risk of death during hospitalization was 34% for both groups, the in-hospital mortality was lower in the control group (34%) than in the treatment group (54%) ( $P = .04$ ; 95% confidence interval, 0.9% to 39.1%). The authors concluded that "use of dobutamine to boost the cardiac index and systemic oxygen delivery failed to improve the outcome in

this heterogeneous group of critically ill patients. Contrary to what might have been expected, our results suggest that in some cases aggressive efforts to increase oxygen consumption may have been detrimental."<sup>21(p1717)</sup>

Later that year, Gattinoni et al<sup>22</sup> published a similar investigation of a much larger group of patients to determine whether increasing the cardiac index to a supranormal level (cardiac index group) or increasing mixed venous oxygen saturation to a normal level (oxygen saturation group) would decrease morbidity and mortality among critically ill patients compared with a control group in which the target was a normal cardiac index. A total of 762 patients belonging to predefined diagnostic categories with acute physiology scores of 11 or higher were randomly assigned to the 2 groups (252 to the control group, 253 to the cardiac index group, and 257 to the oxygen saturation group). The hemodynamic targets were reached by 94.3% of the control group, 44.9% of the cardiac index group, and 66.7% of the oxygen saturation group ( $P < .001$ ). Mortality was 48.4%, 48.6%, and 52.1%, respectively ( $P = .638$ ) up to the time of discharge from the ICU and 62.3%, 61.7%, and 63.8% ( $P = .875$ ) at 6 months. Among patients who survived, the number of dysfunctional organs and the length of the stay in the ICU were similar in the 3 groups. No differences in mortality among the 3 groups were found for any diagnostic category. A subgroup analysis of the patients in whom hemodynamic targets were reached revealed similar mortality rates: 44.8%, 4.4%, and 39.0%, respectively ( $P = .478$ ), and the conclusion was that "therapy aimed at achieving supranormal values for the cardiac index or normal values for mixed venous oxygen saturation does not reduce morbidity or mortality among critically ill patients."<sup>22(p1025)</sup>

Recently, a modification of this kind of strategy using central venous oxygen saturation (ScvO<sub>2</sub>) has become a hot topic of debate. In 2001 Rivers et al<sup>23</sup> reported results of an emergency room study that enrolled 263 patients with severe sepsis and septic shock using goal-directed therapy including ScvO<sub>2</sub> measurement obtained from a central venous catheter. Mortality was significantly reduced from 46.5% to 30.5% ( $P = .009$ ) with implementation of this goal-directed therapy. Criticisms of this study include the perceived lack of treatment that the control group received, the fact that the mortality rates were higher in both groups than would have been predicted by severity illness scoring, and the relatively liberal use of blood

transfusion as a means of increasing the ScvO<sub>2</sub>. A National Institutes of Health-supported multicenter study is currently underway intending to enroll 2000 patients to ascertain whether this strategy is as effective as first reported. If this strategy proves beneficial, the implications of these results to management of later stages of illness will need to be addressed, and goal-directed therapy in the operating room and ICU certainly would be revisited.

In 1996, Connors et al<sup>24</sup> reported on the association between the catheter's use during the first 24 hours of care in the ICU and subsequent survival, length of stay, intensity of care, and cost of care using a prospective cohort study design in 5 teaching hospitals encompassing 5735 critically ill adult patients. Case-matching and multivariable regression modeling techniques were used to estimate the association of right heart catheterization (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. Catheterized patients had statistically significant increased 30-day mortality (odds ratio, 1.24; 95% confidence interval, 1.03-1.49), mean cost, and mean length of stay. There was no subgroup or site for which the catheter was associated with improved outcomes. "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."<sup>24(p889)</sup>

This article, like the article by Gore et al<sup>16</sup> in 1987, was accompanied by an editorial suggesting that perhaps it was time to "pull" the catheter from clinical use.<sup>25</sup>

Subsequently, almost every organized group of physicians involved with patients frequently undergoing catheterization convened, published policy and position papers, and called for better research, particularly in the form of randomized controlled clinical trials. For example, the National Heart, Lung, and Blood Institute and Food and Drug Administration Workshop Report concluded that "areas given high priority for clinical trials were . . . use in persistent/refractory congestive heart failure, acute respiratory distress syndrome, severe sepsis and septic shock, and low-risk coronary artery bypass graft surgery."<sup>26(p2568)</sup>

Since then, only patients undergoing coronary artery bypass surgery have not been subject to significantly better investigation. One early trial of these

patients prospectively examined studied morbidity and mortality in 1094 consecutive patients managed with elective pulmonary artery catheterization ( $n = 537$ ) or with just a central venous pressure catheter (CVP) ( $n = 557$ ).<sup>27</sup> No significant differences in any outcome variables were noted in any group of patients with similar quantitative risk managed with or without a PAC, including those in the highest risk class. This study concluded that the PAC “does not play a major role in influencing outcome after cardiac surgery, that even high-risk cardiac surgical patients may be safely managed without routine PAC, and that delaying PAC until a clinical need develops does not significantly alter outcome, but may have an important impact on cost savings.”<sup>27(p199)</sup> This trial suffered from lack of true randomization and crossover but remains the only large prospective evaluation of PAC use in patients undergoing coronary artery bypass grafting.

A retrospective review by Ramsey et al<sup>28</sup> examined the association between use of pulmonary artery catheterization with hospital outcomes and costs in nonemergent coronary artery bypass graft patients in 56 community-based hospitals in 26 states for a total of 13 907 patients undergoing nonemergent coronary artery bypass graft surgery in 1997. Discharge abstracts for each patient were examined. Stratified and multivariate analyses were used to assess the impact of PACs on in-hospital mortality, length of stay in the ICU, total length of stay, and hospital costs. Outcomes were adjusted for patient demographic factors, hospital characteristics, and hospital volume of PAC use in the year of analysis. Fifty-eight percent of the patients received a PAC. After adjustment, the relative risk of in-hospital mortality was 2.10 for the PAC group compared with the patients who did not receive a PAC (95% confidence interval, 1.40-3.14;  $P < .001$ ).

A more recent retrospective review of outcomes in 2414 low-risk patients undergoing beating heart surgery showed that in the 69% of patients monitored with a PAC versus the 31% with a CVP, there was no change in any outcome variable (eg, need to convert to bypass or insert balloon pump) including mortality rate.<sup>29</sup>

## 2001-2006

In this past 6 years, several large statistically robust investigations have been published. For the sake of organization, these studies are grouped together by the patient population investigated (see Table 2).

## Perioperative Management

In 2003, Sandham et al,<sup>30</sup> representing the Canadian Critical Care Clinical Trials Group, reported the results of a large randomized trial comparing goal-directed therapy using a PAC versus standard care without a catheter, in ASA 3 and higher, 60 years of age and older patients undergoing major surgery followed by ICU admission. This study was carried out in 19 hospitals; 3803 patients were screened and 1994 patients were randomized between 1990 and 1999. Patients randomized to pulmonary artery catheterization had the following goals: oxygen delivery index 550 to 600 mL·min·m<sup>2</sup> of body surface area, cardiac index 3.5 to 4.5 L·min·m<sup>2</sup>, mean arterial pressure 70 mm Hg, wedge pressure less than 18 mm Hg, heart rate less than 120 beats per minute, and hematocrit greater than 27%.

There was no difference in hospital mortality (7.8% vs 7.7%), median length of hospital stay (10 days), cardiac complications including myocardial infarction (4.3% vs 3.4%), congestive heart failure (12.6 vs 11.2), and arrhythmia (9.1 vs 9.3). There were more adverse events in the catheter group (17/994 vs 4/994), mostly related to the risk of inserting and maintaining the catheter itself. The conclusion was that “no benefit to therapy directed by pulmonary-artery catheter over standard care in elderly, high risk surgical patients requiring intensive care [was found].”<sup>30(p5)</sup>

In a study design similar to that of Connors, Polanczyk et al<sup>31</sup> evaluated the relationship between use of perioperative PAC and postoperative cardiac complication rates in patients undergoing major noncardiac surgery. In a prospective, observational cohort design, they investigated 4059 patients in a tertiary care teaching hospital in the United States who underwent major elective noncardiac procedures with an expected length of stay of 2 or more days from 1989 to 1994. Two hundred twenty-one patients had PACs and 3838 did not.

Major cardiac events occurred in 171 patients (4.2%). Patients who underwent perioperative PAC had a 3-fold increase in the incidence of major postoperative cardiac events (34 [15.4%] vs 137 [3.6%];  $P < .001$ ). In multivariate analyses, the adjusted odds ratios (ORs) for postoperative major cardiac and noncardiac events in patients undergoing PAC were 2.0 (95% confidence interval, 1.3-3.2) and 2.1 (95% confidence interval, 1.2-3.5), respectively. In a case-control analysis of a subset of 215 matched pairs of patients who did and did not undergo PAC,

**Table 2.** Clinical Summary of Recent Large Investigations Comparing Management With to Without a Pulmonary Artery Catheter (PAC)

Author/Group	Type	Patient Group	Number of Patients Enrolled	Significant Outcome Differences
Sandham et al (Canadian Critical Care Clinical Trials Group) <sup>30</sup>	Prospective, multicenter	Perioperative	1994	More adverse events in PAC group related to insertion
Polanczyk et al <sup>31</sup>	Observational cohort, single center	Perioperative	4059 total, 215 matched pairs	Increased heart failure and noncardiac events in PAC group after propensity adjustment
Harvey et al (PAC-Man) <sup>32</sup>	Prospective, multicenter	General ICU	1041	None
Rhodes et al <sup>33</sup>	Prospective, single center	General ICU	201	Increased renal insufficiency and thrombocytopenia in PAC group
Sakr et al <sup>34</sup>	Observational cohort, multicenter	General ICU	3147 total, 453 matched pairs	None
Yu et al <sup>35</sup>	Observational, prospective	Severe sepsis	1010 total, 141 matched pairs	None
Binanay et al (ESCAPE) <sup>36</sup>	Prospective, multicenter	Decompensated heart failure	433	Increased infections in PAC group
Richard et al <sup>37</sup>	Prospective, multicenter	ARDS	676	None
ARDS Net <sup>40,41</sup>	Prospective, multicenter	ARDS	PAC 501, CVC 480	Increased catheter-related complications and blood transfusions in PAC group

ICU = intensive care unit; ARDS = acute respiratory distress syndrome; CVC = central venous catheter.

adjusted for propensity of PAC and type of procedure, patients who underwent perioperative PAC also had increased risk of postoperative congestive heart failure (OR 2.9; 95% confidence interval, 1.4-6.2) and major noncardiac events (OR 2.2; 95% confidence interval, 1.4-4.9). The study formally concluded that "no evidence was found of reduction in complication rates associated with use of perioperative [PAC] in this population"<sup>31(p309)</sup>; in actuality, complication rates were increased and heart failure was more likely to have occurred in the patients managed with a PAC than those who were not.

### Intensive Care

In 2005, the PAC-Man study collaboration reported the results of a randomized controlled trial of 1041 patients managed in 65 U.K. ICUs between 2001 and 2004.<sup>32</sup> The timing of PAC insertion and management of patients entered were not algorithmically determined but instead were left to the individual clinician.

Some patients managed without a PAC were monitored with other cardiac output monitoring devices. The main reason for management of patients in this study was the desire to guide inotropic or vasoactive drug treatment already in progress (72% of study entrants).

There was no difference in hospital mortality (68% in PAC group vs 66% in non-PAC group). Hospital mortality was the same in the non-PAC group whether an alternative cardiac output monitoring device was used. No subgroup based on either Acute Physiology and Chronic Health Evaluation (APACHE) II risk of death, major presumptive clinical syndrome, or the unit's frequency of PAC use showed an improved outcome. Outcomes other than hospital mortality, such as length of stay in the ICU or the hospital and days of organ support in the unit, were also the same in the 2 groups. Management was changed in 80% of catheterized patients after catheterization. Notably, 46 of the 486 PAC patients experienced a device-related complication, none of which was fatal. The authors concluded

that there was “no clear benefit, or harm by managing critically ill patients with a PAC.”<sup>32(p472)</sup>

Earlier, in a much smaller single-center randomized controlled clinical trial from 1997 to 1999, Rhodes et al<sup>33</sup> compared the survival and clinical outcomes of critically ill patients treated with the use of a PAC with those treated without the use of a PAC in 1 teaching hospital's ICU. Two hundred one critically ill patients were randomized to either the PAC ( $n = 95$ ) or the control group ( $n = 106$ ). There was no significant difference in mortality between the PAC group (46/95, 47.9%) and the control group (50/106, 47.6) (95% confidence interval for the difference,  $-13\%$  to  $14\%$ ,  $P > .99$ ). The mortality rate for participants who had management decisions based on information derived from a PAC was 41 of 91 (45%, 95% confidence interval,  $-11\%$  to  $16\%$ ,  $P = .77$ ). The PAC group had significantly more fluids in the first 24 hours (4953 vs 4292) and an increased incidence of renal failure (35% vs 20% of patients at day 3 postrandomization,  $P < .05$ ) and thrombocytopenia ( $P < .03$ ). Although the authors concluded that “these results suggest that the PAC is not associated with an increased mortality,”<sup>33(p256)</sup> there was an increased morbidity—renal insufficiency and thrombocytopenia both occurred in the PAC group with statistically significant greater frequency.

In another cohort study, this one in 198 European ICUs participating in the Sepsis Occurrence in Acutely Ill Patients Study, 3147 adult patients admitted to 1 of the participating ICUs between May 1, 2002, and May 15, 2002, were classified according to whether they had a PAC at any time during their ICU stay and were followed up until death, to hospital discharge, or for 60 days.<sup>34</sup> Propensity score case matching was performed, and matched pairs were examined for baseline characteristics and outcome. Of 3147 patients, 481 patients (15.3%) had a PAC. Patients with a PAC were older, had a higher incidence of heart failure, had a lower incidence of cancer, and were more commonly surgical admissions. Fluid balance was comparable between the 2 groups. ICU and hospital mortality rates were higher in patients with a PAC (28.1% vs 16.8% and 32.5% vs 22.5%, respectively;  $P < .001$ ). However, PAC use was not an independent risk factor for 60-day mortality in multivariate analysis, and in 453 propensity-matched pairs, ICU and hospital mortality rates were comparable between groups (26.7% vs 26.3% and 31.4% vs 32.8%,  $P =$  not significant). The conclusion of this observational study was

that PAC use was not associated with increase in mortality in this heterogeneous population.

In another case-control cohort study, again similar to that of Connors et al,<sup>24</sup> the relationship of PAC use to patient outcomes, including mortality rate and resource utilization, was studied in 1010 patients with severe sepsis in 8 academic medical centers.<sup>35</sup> The case-matched subset of patients included 141 pairs managed with and without the use of a catheter. The mortality rate was not statistically significantly lower among the group managed with a PAC compared with those not managed with one (41.1% vs 46.8%,  $P = .34$ ), and when adjusted for comorbidities and severity of illness the adjusted odds ratio was 1.02 (95% confidence interval, 0.61-1.72). Similar analysis accounting for comorbidities and severity of illness led to the conclusion that “among patients with severe sepsis, PAC placement was not associated with a change in mortality rate or resource utilization.”<sup>35(p2734)</sup>

### Decompensated Heart Failure

The evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness (the ESCAPE trial) was funded by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health.<sup>36</sup> It was designed to determine the safety and clinical effect of catheterization in patients hospitalized with severe symptomatic and recurrent heart failure. Between 2000 and 2003, 433 patients from 26 sites were randomized to receive either a PAC plus clinical assessment-guided therapy or clinical assessment alone. If a catheter was inserted, the goal was to lower the wedge pressure to less than 15 mm Hg and the right atrial pressure to less than 8 mm Hg. Clinical resolution of pulmonary congestion was the main clinical goal.

There was no difference in mortality, length of hospitalization, or days alive and out of the hospital at 6 months. Although more in-hospital adverse events occurred in the PAC group, most commonly infection (in 4 of the 215 PAC patients), there were no deaths related to PAC use. The article concluded that “therapy to reduce volume overload during hospitalization for heart failure led to marked improvement in signs and symptoms of elevated filling pressures with or without a PAC.”<sup>36(1625)</sup> Notably, 11% of its patients enrolled in the PAC-Man trial had heart failure, and in that subgroup too, there was no difference in outcome endpoints.

## Adult Respiratory Distress

A multicenter (36 participants) randomized controlled study of 676 adult patients from 1999 to 2001 performed in France was designed to determine the effects on outcome of the early use of a PAC in patients with shock mainly of septic origin, acute respiratory distress syndrome (ARDS), or both.<sup>37</sup> Patients were randomly assigned to either receive a PAC (n = 335) or not (n = 341), and treatment was left to the discretion of each individual physician. The 2 groups were similar at baseline. There were no significant differences in mortality with or without a PAC at day 14, 49.9% versus 51.3% (relative risk, 0.97; 95% confidence interval, 0.84-1.13;  $P = .70$ ); day 28, 59.4% versus 61.0% (relative risk, 0.97; 95% confidence interval, 0.86-1.10;  $P = .67$ ); or day 90, 7.7% versus 72.0% (relative risk, 0.98; 95% confidence interval, 0.89-1.08;  $P = .71$ ). At day 14, the mean number of days free of organ system failures with or without a PAC ( $2.3 \pm 3.6$  vs  $2.4 \pm 3.5$ ), need for dialysis ( $7.4 \pm 6.0$  vs  $7.5 \pm 5.9$ ), and need for vasoactive agents ( $3.8 \pm 4.8$  vs  $3.9 \pm 4.9$ ) did not differ. Also, length of stay in the ICU ( $3.4 \pm 6.8$  vs  $3.3 \pm 6.9$ ) and days of mechanical ventilation required ( $5.2 \pm 8.5$  vs  $5.0 \pm 8.5$ ) were not different. The conclusion was that "management involving the early use of a PAC in patients with shock, ARDS, or both did not significantly affect mortality and morbidity."<sup>37(p2713)</sup>

All of these trials, as well as some others of less importance to anesthesiologists, are well summarized in a meta-analysis that appeared in the same issue of the *Journal of the American Medical Association* as the ESCAPE trial.<sup>38</sup> The meta-analysis and accompanying editorial<sup>39</sup> both concluded that no patient group appears to benefit from PAC.

The most recently published large, multicenter, randomized prospective PAC trials are the 2 studies conducted by the NIH ARDS Clinical Trials Network titled Pulmonary Artery Catheter Versus Central Venous Catheter to Guide Treatment of Acute Lung Injury<sup>40</sup> and Comparison of Two Fluid-Management Strategies in Acute Lung Injury.<sup>41</sup> These 2 studies used a  $2 \times 2$  factorial design to randomize patients with acute lung injury to simultaneously receive either a PAC or central venous catheter (CVC) and either conservative or liberal use of fluids. The goals were to (1) assess the safety and the efficacy of PAC versus CVC-guided management in reducing the need for mechanical ventilation, morbidity, and mortality in patients with acute lung injury; and (2) assess the safety and efficacy of "fluid-conservative" versus "fluid-liberal" management strategies on lung function, the need for

mechanical ventilation, length of stay, nonpulmonary organ function, and mortality.

There were 1001 patients with acute lung injury for 48 hours or less who were randomized to either group: 501 received a PAC and 480 received a CVC. A standard management protocol was followed using specific clinical (eg, blood pressure, urine output) and hemodynamic variables (pulmonary artery occlusion, or wedge, pressure [PAOP] and cardiac index from PAC, CVP plus clinical assessment of skin for circulatory effectiveness in the CVC group) to guide either a fluid-liberal or fluid-conservative approach. The protocol was used in patients not in shock (shock was defined as a systolic pressure <60 mm Hg). The overriding goals were prompt reversal of hypotension, oliguria, and ineffective circulation so that patients in shock received resuscitation based on the primary physicians' recommendations. The hemodynamic protocol was followed for 7 days or 12 hours after discontinuation of assisted breathing; however, the PAC could be discontinued after 3 days and replaced by CVC-guided fluid management if hemodynamic stability (no need for protocol-directed interventions) was achieved. Approximately 90% of protocol instructions were followed with a 1% crossover from CVC- to PAC-guided therapy, indicating that the objectives for study design were met.

The primary outcome measure in the PAC versus CVC trial, mortality during the first 60 days before discharge home, was not significantly different (27.4% vs 26.3% respectively;  $P = .69$ ; 95% confidence interval, -4.4% to 6.6%).<sup>38</sup> Within the first 28 days, ventilator-free days ( $13.2 \pm 0.5$  and  $13.5 \pm 0.5$ ;  $P = .58$ ) and days not spent in the ICU ( $12.0 \pm 0.4$  and  $12.5 \pm 0.5$ ;  $P = .40$ ) were not different. Of additional clinical significance, PAC use was not associated with reduction in organ system failure or the need for life support even in the subgroup of patients with shock at study entry. Fluid balance and the use of diuretics and fluids were similar in both groups; however, the PAC group received significantly more erythrocyte transfusions (38% vs 30%,  $P = .008$ ). The PAC group had approximately twice as many catheter-related complications, mainly arrhythmias.

In the study arm to assess the safety and efficacy of a fluid-restrictive versus a fluid-liberal management in acute lung injury,<sup>39</sup> there was no significant difference in mortality (25.5% vs 28.4%,  $P = .30$ ; conservative vs liberal); however, the conservative fluid management significantly decreased the lung injury score and increased the oxygenation index, the number of ventilator-free days, and the number

of days not spent in the ICU during the first 28 days. These differences were only related to treatment protocol, not whether a PAC or CVC was inserted.

## Why Do PACs Fail to Improve Patient Outcome?

### Patient Selection

There are several explanations why PACs do not have a positive effect on outcome. If the catheter does improve hemodynamic management, some patient groups are simply either too well or too sick for this improvement in hemodynamic management to change outcome. For example, in the trials involving peripheral vascular disease,<sup>9,10,12</sup> infrarenal abdominal aortic aneurysm repair,<sup>7,8,10-12</sup> and especially low-risk coronary artery bypass,<sup>27-29</sup> mortality rates are already so low (eg, <3%) that improved hemodynamic management is unlikely to have a demonstrable impact. Benefit is even less likely to result when 1 of the main postoperative morbidities, myocardial infarction, has been reduced in incidence by rigorous preoperative screening, perioperative administration of  $\beta$ -blockers, and postoperative administration of aspirin and other anticoagulants.

Another reason that the catheter may fail to improve outcomes is that it is used to monitor patients with diseases such as septic shock, ARDS, and multiple organ failure. These conditions not only carry very high mortality rates (eg, >40%) but also have as their mainstay of care treatments that are not directly influenced by hemodynamic data provided by the PAC. The authors of this article refer to the term "contextual hemodynamics" to describe what is genuinely practiced. For example, the clinician's desire to increase cardiac output may be determined by the heart rate, blood pressure, hemoglobin level, serum lactate level, presence of pulmonary edema, renal function, cardiac ischemia or perceived risk for ischemia, cerebral and mesenteric circulation, and age. A PAC will provide only 2 or 3 of perhaps a dozen or more variables that will be taken into account in determining a management strategy. Furthermore, the PAC is an invasive monitor and it is possible that any benefits are mitigated by the potential morbidity and mortality associated with its complications.<sup>42</sup>

### Utility of the Data

The hemodynamic variables obtained by the PAC include the systolic and diastolic pulmonary artery

pressures, the PAOP, and the thermodilution cardiac output (CO). Although CVP is also obtained simultaneously, its measurement does not uniquely require a PAC and will not be discussed here.

PAOP is still considered by most physicians to be the most important variable derived from the PAC<sup>43</sup> and clinically is the most frequently used measurement. It is commonly used as an index of left ventricular filling and intravascular volume. It has become ingrained in the lexicon of cardiac physiology, and in numerous clinical studies it has been used to demonstrate ventricular function (eg, Starling curves by plotting left ventricular stroke work vs PAOP) and serves in protocols to determine critical hemodynamic management decisions.<sup>44</sup> It is also used as a diagnostic criterion (eg, the differentiation of cardiogenic vs noncardiogenic pulmonary edema).<sup>45</sup> For instance, in a recent randomized prospective study of PAC, use of PAOP in the ICU was determined every hour to guide decision making.<sup>33</sup>

Despite these advocated uses, there is no evidence that PAOP is an index of left ventricular filling, preload, or intravascular volume. In fact, the PAOP may be the least useful piece of data emanating from the PAC (see Table 3).

Clinically, preload is equated to the volume of blood in the left ventricle measured at end-diastole (ie, the left ventricular end-diastolic volume [LVEDV]). The physiological relationships between pressure (LVEDP) and volume (LVEDV) have been traditionally graphed as ventricular compliance curves. However, in patients with cardiac disease or critical illness<sup>46-48</sup> and even in volunteers with normal hearts,<sup>49</sup> this compliance curve cannot be demonstrated using PAC-derived PAOP. There is also no relationship between PAOP and intravascular volume measured by radionuclide technique.<sup>50</sup> Traditional thinking that fluid challenges and trended serial changes in PAOP are useful management tools has also been recently challenged.<sup>49</sup> In a study by Kumar et al<sup>49</sup> of normal volunteers subject to acute volume loading, filling pressures were shown to variably decrease, increase, or not change over time, and the filling pressures had no correlation with cardiac output. It is clear that PAOP measurement will not allow the clinician to estimate filling of the heart or overall intravascular volume in sick patients with abnormal ventricular function who perhaps have conditions such as underlying hypertrophic myocardium secondary to hypertension; valvular disease; acute changes in wall stiffness attributable to ischemia or to inotrope, vasoconstrictor, or vasodilator administration; rapidly changing intrinsic hormonal and catecholamine activity; positive pressure

**Table 3.** Selected Studies Analyzing the Measured Pulmonary Artery Occlusion Pressure (PAOP)

Study	Variable Measured: Investigation	Results
Baek et al <sup>50</sup>	Blood volume: PAOP vs radionuclide	No correlation
Raper et al <sup>48</sup>	LV preload: PAOP vs radionuclide	No correlation
Fontes et al <sup>46</sup>	LV preload: PAOP vs TEE determination	No correlation
Kumar et al <sup>49</sup>	LV preload: PAOP vs radionuclide or TTE	No correlation
Nemens and Woods <sup>53</sup>	PAOP: variability every 5 min over 30 min (ventilated ICU patients)	60% <4 mm Hg, 40% = 4-7 mm Hg
Al-Kharrat et al <sup>54</sup>	PAOP variability: interobserver range	-11 mm Hg to 15 mm Hg
Rizvi et al <sup>55</sup>	PAOP agreement in assessment: within 2 mm Hg	71% to 83% (see text)
Iberti et al <sup>56</sup>	PAOP: physician interpretation of tracing	47% incorrect
Hansen et al <sup>47</sup>	Starling curve using PAOP; Starling curve using radionuclide LV preload	Not present; present
Kumar et al <sup>49</sup>	Starling curve, presence using PAOP; Starling curve, presence using echo-derived LV area	Not present; present

LV = left ventricular; TTE = transthoracic echocardiography; TEE = transesophageal echocardiography; ICU = intensive care unit.

ventilation; positive end-expiratory pressure; and changes in intra-abdominal pressure.

One dramatic clinical example of the limitation of the PAOP as an indicator of preload is the entity of dynamic left ventricular outflow tract obstruction.<sup>51</sup> In this condition, a patient with hypotension, elevated PAOP, and low CO is often incorrectly treated with increasing doses of inotropes and vasopressors in an effort to improve blood pressure, lower PAOP, and increase CO. As the dosages of these medications are increased, the PAOP increases, the CO or stroke volume decreases, and the patient remains tachycardic and hypotensive. A diagnosis of refractory heart failure seems reasonable and many clinicians would interpret the PAC readings as indicative of hypocontractile heart. However, echocardiography reveals a hyperdynamic empty ventricle with severely decreased preload and systolic anterior motion of the anterior mitral valve leaflet, obstructing the aortic outflow tract and leading to dynamic left ventricular outflow tract obstruction. Despite the high PAOP and pulmonary edema, the treatment is vigorous fluid resuscitation and withdrawal of vasoactive agents. The outflow tract obstruction is completely reversible. The diagnosis cannot be made by PAC but can be readily recognized by echocardiography.

Even the extended-function PACs that estimate right ventricular end-diastolic volume (RVEDV) using gated thermodilution measurements of temperature change per beat have been shown by transesophageal echocardiography to overestimate LVEDV by 2 to 3 times actual volume,<sup>52</sup> and if PAC-derived RVEDV is

relied on as an index of LV preload, these catheters may lead to underresuscitation.

PAOP may not reflect true LVEDP either. At best, after inflation of the balloon, occluding blood flow distal to the tip of the PAC in the pulmonary artery, the pressure at this point (PAOP) should be equal to the pulmonary capillary pressure, which in turn is equal to the pulmonary venous pressure, which is equal to the mean left atrial pressure, which is equal to the LVEDP. However, there are a multitude of reasons why PAOP may not be equal to LVEDP, including significant pulmonary parenchymal or vascular disease that prevents accurate reading of the pressures across the pulmonary bed; location of the PAC tip in a West zone 1, which will lead to mistaken measurement of alveolar pressure; high transmural pressures generated from positive intrathoracic or intra-abdominal pressure; mitral valve disease; tachycardia; eccentric balloon inflation; catheter kinking or air bubbles; errors in zeroing and calibration; and inconsistency in estimation of pressure attributable to respiratory variation.

## Data Acquisition and Interpretation

Perhaps the most significant source of error in the PAOP is caused by significant respiratory fluctuations in the waveform, rendering determination of pressures difficult or even impossible. In mechanically ventilated hemodynamically stable patients, when the PAOP was determined every 5 minutes for 30 minutes, 60% fluctuated by less than 4 mm Hg,

but 40% varied by 4 to 7 mm Hg in the absence of any apparent clinical changes.<sup>53</sup>

Significant differences exist in PAOP interpretation between intensivists, cardiologists, and ICU nurses, with interobserver variability ranging from -11 mm Hg to 15 mm Hg.<sup>54</sup> In the recently published ARDSnet trial, agreement within 2 mm Hg occurred in only 71% of measurements when an airway pressure tracing was absent from the strip chart recording of the PAOP.<sup>55</sup> Even when the airway pressure tracing was added, agreement only improved to 83%.

More important, almost half of physicians queried using a formal written examination were unable to accurately determine the PAOP from a clear printed tracing.<sup>56</sup> Considering these known difficulties in PAOP interpretation, it is not surprising that there is significantly higher interobserver agreement in diagnosis using echocardiographic versus PAC monitoring in postoperative cardiac surgical patients.<sup>57</sup> A recent survey of practicing cardiac anesthesiologists concluded that "a large proportion of anesthesiologists who use the PAC disagree about PAOP estimation, and even those who agree may lack the confidence necessary to use it effectively."<sup>58(p1203)</sup>

There remains the widespread belief that even if the PAOP does not reflect LV preload or volume or intravascular volume, it may help to determine the etiology of pulmonary edema (eg, cardiogenic vs noncardiogenic) by reflecting the hydrostatic pulmonary capillary pressure, a determinant of edema formation. In practice, however, the PAOP may not reflect the true pulmonary capillary pressures, which may be higher than PAOP if pulmonary vascular resistance is elevated.<sup>59</sup> In addition, other variables determine edema formation, especially the degree of capillary leak secondary to endothelial injury and inflammation, the serum oncotic pressure, and the changing lymphatic drainage capacity.

To highlight this potential error in application, note that in the NIH ARDS Clinical Trials Network PAC versus CVC trial, in 29% of the patients with a PAOP greater than 18 mm Hg, the traditional threshold used to differentiate noncardiogenic from cardiogenic pulmonary edema, 97% of patients had a normal or elevated cardiac index and therefore may not have had cardiogenic pulmonary edema as was reported!<sup>40</sup>

Starling curves are based on Starling's "law of the heart," the observation that the length or stretch of the cardiac muscle fibers determines the strength of contraction.<sup>60,61</sup> It is but 1 of many factors, including heart

rate, intrinsic contractility, myocardial muscle elastance, and local neurohumeral activity, that can influence cardiac performance and tends to be most easily demonstrated in *ex vivo* isolated heart preparations. The determination of the length of cardiac muscle fibers is not directly possible in patients, so ventricular filling or preload became a surrogate for muscle length. Pressure (ie, PAOP) was then eventually substituted for volume (ie, LVEDV), because it was easier to measure and more readily available.<sup>61</sup> Using the PAC, the clinician plots cardiac performance (using stroke volume or stroke work) against a measure of cardiac muscle length, in this case PAOP. However, if PAOP does not reflect LVEDV, then Starling curves should not be demonstrable when using PAOP to construct them. In fact, it has been shown that Starling curves cannot be demonstrated using PAC-derived PAOP,<sup>46-49</sup> even though some investigations have claimed to use this curve to optimize patients.<sup>6</sup>

Inaccuracies of the PAOP should also be considered when using formulas that use PAOP in their calculations, such as pulmonary vascular resistance and left ventricular stroke work. If the PAOP is inaccurate in terms of estimating the true LVEDP, the derived parameter is also inaccurate. Therefore, on this basis alone it is clear why PAC-derived variables, such as the LVSWI, poorly correlate with direct echocardiographic assessment of global contractility and regional wall motion.<sup>62</sup>

Thermodilution cardiac output (TDCO) is a more reliable and accurate hemodynamic parameter compared with PAOP; however, it may be subject to error in the case of tricuspid regurgitation, concomitant intravenous infusions, inaccurate injectate volume, and respiratory cycle variation, among other factors.<sup>63,64</sup> Recently it has been demonstrated that pneumatic compression devices, now used commonly to prevent deep vein thrombosis but not in use when TDCO was introduced, can falsely lower TDCO measurements by as much as 48%.<sup>65</sup>

## Conclusion

No patient group has been demonstrated to benefit from pulmonary artery catheterization, and there is overwhelming evidence that the PAOP may be unreliable, inaccurate, and misinterpreted to such a degree as to be a potentially harmful parameter on which to base clinical decisions.

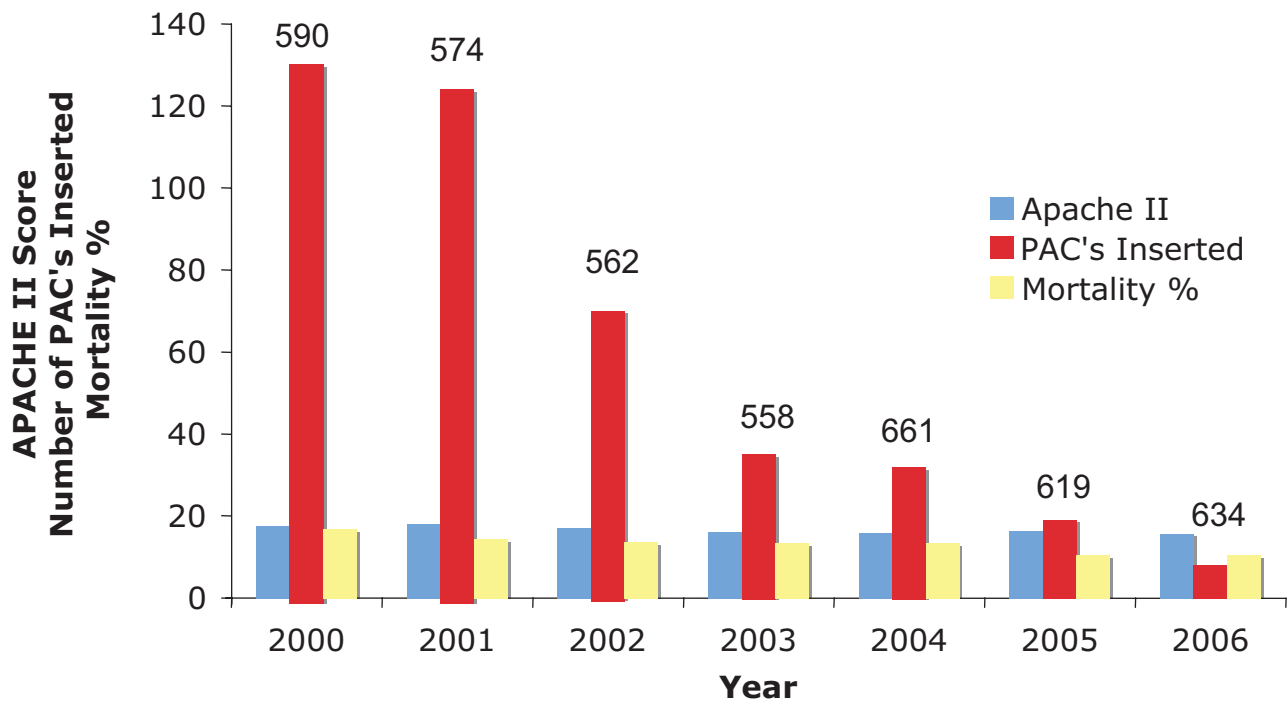


Figure 1. Mount Sinai surgical intensive care unit data. PAC = pulmonary artery catheter; APACHE = Acute Physiology and Chronic Health Evaluation. The number of patients admitted per year is noted about the center bar (range 558-661).

As of 2002, the PAC was the most frequently used and preferred monitor among cardiovascular anesthesiologists.<sup>67</sup> However, since then, several well-designed large prospective and retrospective investigations have repeatedly demonstrated that PACs at best are associated with no increase in morbidity and mortality. Notably, several of these investigations were designed and carried out by historically staunch proponents of pulmonary artery catheterization.

Recently emerging applications of perhaps greatest interest to anesthesiologists include perioperative management of the patient with pulmonary artery hypertension and use as a "rescue" monitor for patients failing routine hemodynamic supportive measures. These 2 patient groups are relatively small, and it is unlikely that any large-scale trial can be performed in them.

There may also be an almost insurmountable educational challenge. Assuming that PACs are used in only very unusual scenarios and given the already poor fund of knowledge among physicians, who use PACs with much greater frequency than limiting use to these scenarios will allow, then how can skills be even maintained, let alone possibly improved?

Although this challenge looms, it is very likely that competing monitoring modalities, especially echocardiography, pulse contour analysis, and non-invasive cardiac output determination, will significantly reduce the number of PACs inserted.

For example, in our surgical ICU, which admits approximately 600 perioperative patients per year with an average APACHE II score of 16.5, over the past 5 years we have reduced the number of PACs inserted from 134 per year to only 8 last year, while slightly reducing ICU and hospital mortality, which was already less than predicted by APACHE II score (see Figure 1). This experience will likely become the norm.

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