Role of the Pulmonary Artery Catheter in Diagnosis and Management of Heart Failure

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KEYWORDS

- Decompensated heart failure
- Pulmonary artery catheter • Swan-Ganz catheter
- Congestive heart failure • Management of heart failure

Almost 4 decades have passed since the introduction of the balloon-tipped, flow-directed pulmonary artery catheter (PAC) by Swan and colleagues.[1] This technical achievement transformed the pulmonary artery catheter from a laboratory device into a practical bedside tool capable of providing continuous central hemodynamic monitoring. The PAC, once defined as "the cornerstone of the intensive care units" and regarded as an important management tool, has faced noteworthy scrutiny in the past 2 decades. Starting in the late 1980s, several reports raised concern about the actual impact of pulmonary artery catheter use on improving clinical outcomes.[2–4] Concerns intensified after a large retrospective observational trial suggested possible harm associated with the use of PAC.[5,6] Several prospective studies were then performed to evaluate the outcomes of PAC use in a variety of acute medical and surgical conditions,[7–12] including decompensated chronic heart failure.[13] Despite differences in study designs and heterogeneities of studied populations, results from these randomized clinical trials have consistently shown lack of any measurable outcomes benefit from the routine use of PACs in critically ill patients. Consequently, PACs in clinical practice have undergone a steep decline in use. Between 1993 and 2004, PAC use has decreased by up to 65% for all medical admissions in many institutions, with the sharpest decline seen in the management of acute myocardial infarction (81%), acute respiratory failure (76%), and septicemia (54%) (**Fig. 1**).[14]

This article addresses the role of PACs in the diagnosis and management of heart failure, the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial and registry, the impact of ESCAPE and related studies on the practical management of heart failure, and the general indications for PAC application in current clinical practice.

TECHNICAL EVOLUTION OF THE PULMONARY ARTERY CATHETER

The PAC is an interesting tool that enjoyed an exciting journey from the time it was discovered up to current times. By act of an inadvertent exploration, Forssmann was first to establish the concept of right heart catheterization in 1929.[15] With the intent to deliver drugs directly into the heart, Forssmann advanced a ureteral catheter into his own heart by accessing an "elbow vein" (likely antecubital), and confirmed the presence of the catheter's tip in his right atrium with an

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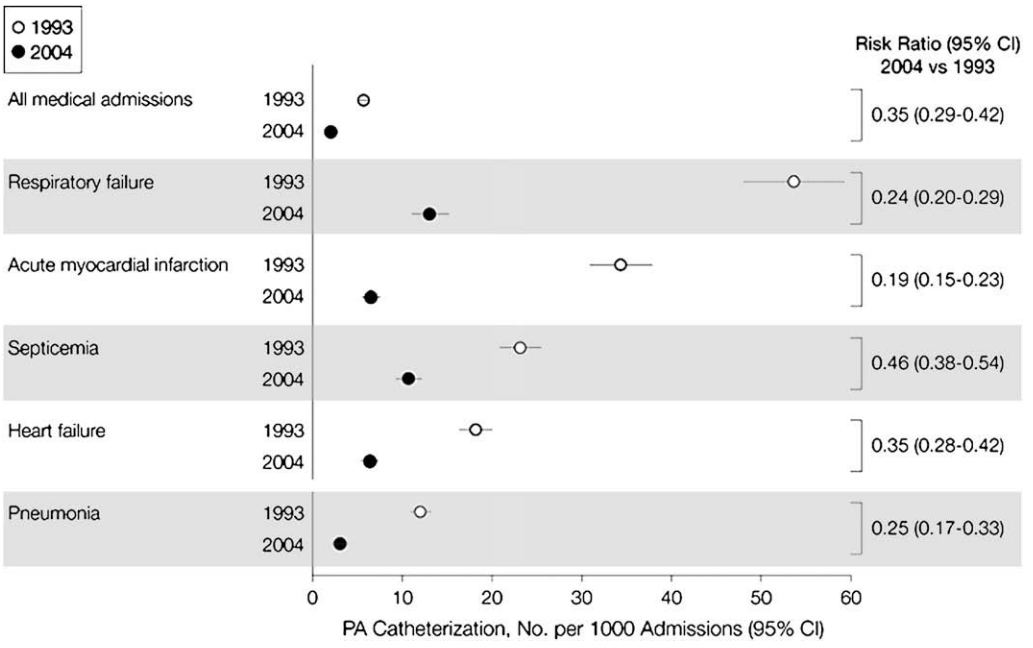

Fig. 1. Trend in pulmonary artery catheter use between 1993 and 2004 according to pre-identified diagnoses. PA, pulmonary artery; CI, confidence intervals. (*From* Wiener RS, Welch HG Trends in the use of the pulmonary artery catheter in the United States, 1993–2004. JAMA 2007;298:423–9; with permission.)

x-ray image; this event is regarded by many as the birth of cardiovascular catheterization.

About a decade later, Cournand and Richards[16–18] expanded the use of the right heart catheter to measure right heart pressures and cardiac output. Their work also provided a better understanding of cardiopulmonary hemodynamics and gas exchange. In 1956, Forssmann, Cournand, and Richards received the Nobel Prize in Medicine for their work in the development of the PAC. Although measurement of pulmonary capillary wedge pressure was first described in 1949 by Hellems and colleagues,[19] the link between the pulmonary wedge pressure and the left atrial pressure, however, was established in 1954 by Connolly and colleagues.[20]

After its introduction in the mid 1940s, the PAC remained investigational and confined to the catheterization laboratories for research purposes and limited clinical diagnoses. Over the following years, two major challenges remained to be solved for the PAC: first, the ability to obtain continuous recordings of human central hemodynamics; and second, transferring the use of the PAC from the research and diagnostic laboratories to the patient's bedside. In 1970, both challenges were achieved by H.J.C. Swan and colleagues,[1] who added a balloon to the catheter tip of the standard PAC, allowing blood flow–directed movement and positioning. This novel idea has indeed shaped the future of this device. Balloon-tipped PACs not only provided clinicians with the ease and safety of bedside placement via floatation of the catheter tip upstream, it enabled them to measure right atrial pressure and PA pressure continuously and pulmonary capillary wedge pressure intermittently via inflation and deflation of the balloon. About a year later, W. Ganz and colleagues[21] added a thermistor to the tip of the catheter allowing direct measurement of cardiac output by thermodilution technique (using temperature as the indicator). For their renowned contribution to the advancement of this clinical tool, medical communities worldwide began to refer to the PAC as the "Swan-Ganz catheter."

CLINICAL TRIALS THAT SHAPED THE HISTORY OF THE PULMONARY ARTERY CATHETER

When Swan and Ganz launched their balloon-tipped, flow-directed PAC in 1970, the use of PACs expanded considerably and gained in popularity. Physicians now had a means to perform continuous monitoring of central hemodynamics (eg, pulmonary artery pressure, pulmonary wedge pressure, and cardiac output). PAC use was initially directed at the care of patients with acute myocardial infarction, shock, or heart failure, and later extended to surgical units, despite the lack of any solid scientific evidence to support its

widespread clinical application. In 1976, the Medical Device Amendments were added to the Food, Drug, and Cosmetic Act of 1938, establishing the branch for Devices and Radiological Health of the Food and Drug Administration (FDA); the intent was to evaluate and regulate the application of medical devices in clinical practice. However, because of some exceptions in rulings, the PAC escaped intense investigation and scrutiny early in its development and its use then proceeded without strict regulation.

In the mid 1970s, reports by Forrester and colleagues[22,23] supported the regular application of PACs in patients with myocardial infarction complicated by hemodynamic instability. Their conclusions were complemented by Rao and colleagues[24] who retrospectively investigated the impact of PACs on reducing perioperative mortality between 1973 and 1976 and prospectively between 1977 and 1982; they found a significant decrease in the rate of perioperative myocardial infarction, from 7.7% to 1.9% ($P < .005$) in patients who required PACs to guide therapy. Additional favorable reports followed and contributed to the surge in the popularity of this device over the ensuing 20 years.[25,26]

The golden era for PACs, however, was disrupted by the first large negative study published in 1987 by Gore and colleagues.[5] Although the study was a retrospective look, the results indicated that PAC use may be associated with an increased mortality in patients hospitalized for acute myocardial infarction complicated by congestive heart failure (CHF), hypotension, and/or cardiogenic shock. In their retrospective investigation of 3263 patients, hospital mortality was 44.8% in heart failure patients selected to be managed with a PAC compared with 25.3% in those who did not receive a PAC ($P < .001$). Among hypotensive patients, PAC use was associated with a 48.3% mortality compared with 32.2% in the non-PAC hypotensive group ($P < .001$). Shock patients did poorly in both groups with mortality of 74.4% in the PAC group and 79.1% in the non-PAC group (not different statistically). PAC use was also associated with a longer duration of hospitalization. Among survivors at hospital discharge, 5-year mortality was the same in both groups. This study has been heavily criticized for its retrospective chart review, case control design, and lack of risk adjustment. Furthermore, it is hard to identify one intervention (PAC use) as causal in such high-risk patients. The accompanying editorial by Robin,[6] encouraged more rigorous investigation in the use of PACs in clinical practice. At that point in time, 20% to 43% of all patients admitted to critical care units underwent placement of PACs during their stay.[5,27]

Within a decade, prospective studies regarding PAC use started to unfold. Connors and colleagues[7] prospectively studied the relationship between PACs and outcomes (mortality and length of stay) and cost of care in critically ill patients. Results showed that patients managed with PACs within 24 hours of admission had a significantly increased 30-day mortality (odds ratio [OR]: 1.24; 95% confidence interval [CI], 1.03-1.49), higher hospital costs, and longer length of stay. This study and the accompanying editorial by Dalen and Bone,[28] were among those that led the Heart, Lung, and Blood Institute of the National Institutes of Health to call for workshops to further examine the clinical application of PAC use in all areas of clinical medicine. From there, the Evaluation Study of Congestive Heart Failure and Pulmonary Artery catheterization Effectiveness (ESCAPE) Trial[29] was developed and conducted as the first prospective randomized trial designed to assess the benefits of PAC use in managing patients with advanced symptomatic congestive heart failure.

PULMONARY ARTERY CATHETERS IN HEART FAILURE POPULATIONS

Basic Management Concepts in the Pre-Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness Era

Before we discuss ESCAPE, it is important to address some of the approaches to managing decompensated heart failure in the pre-ESCAPE trial era. The concept of ''tailored therapy'' was developed for patients with decompensated heart failure. With the ultimate goal of relieving the symptoms of congestion and volume overload, tailored therapy is a strategy that involves using PAC-derived hemodynamic data to guide therapy and achieve optimal hemodynamic responses to administered dosing of intravenous agents (eg, nitroprusside, nitroglycerin); thereafter, oral medications were adjusted to match the optimal response. Proponents of this approach have advocated that optimal hemodynamics via PAC-monitored selection of the best drugs (and at the most appropriate doses) would lead to optimal clinical outcomes. Preliminary studies showed that tailored therapy may improve cardiac performance, functional status, and heart failure symptoms and lead to better outcomes in patients with lower filling pressures at discharge.[30–32] The lack of a randomized, parallel non-PAC control arm was a major limitation of these studies.

The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness Trial and Registry

The ESCAPE trial[13] was the first prospectively randomized, controlled multicenter trial designed to evaluate the use of the PAC in hospitalized patients with advanced heart failure. The study intent was to determine whether the addition of PAC-guided therapy to clinical assessment would further enhance outcomes (reduce mortality and hospitalizations) over therapy guided by clinical assessment alone in patients with advanced symptomatic heart failure. A total of 26 study centers with very experienced heart failure specialists in the United States and Canada participated in this trial between 2000 and 2003. A total of 433 patients were enrolled with goals of relieving clinical congestion and improving symptoms in both treatment groups. Patients were randomly assigned to the clinical assessment group, for which therapeutic decisions were guided by clinical assessment alone or to the pulmonary artery catheter group, for which therapy was guided by clinical assessment in addition to central hemodynamic data provided by the PAC. Entry criteria included severely symptomatic heart failure and overt signs of congestion, for which PAC use was felt to be beneficial for management; however, patients still had to be stable enough so that PAC management would not be absolutely necessary or mandatory. Patients with advanced renal failure and those who required intravenous inotropic agents for clinical stabilization were excluded from the trial. The overall target of therapy in both groups was the resolution of signs and symptoms of clinical congestion, but in the PAC group, a pulmonary artery capillary wedge pressure of 15 mm Hg or less and right atrial pressure of 8 mm Hg or less were also targeted. The primary trial end point was the total number of days alive out of the hospital in the first 6 months after enrollment. Secondary end points included exercise tolerance, quality of life, and echocardiographic measurements.

Both groups experienced improvement in symptoms and signs of congestion, and there was no statistical difference in the primary end point. The number of days alive out of the hospital in the first 6 months between the clinical assessment and the PAC group were 133 days and 135 days respectively, with a hazard ratio of 1.00 (95% CI: 0.82-1.21) (**Fig. 2**). Mortality at 6 months did not statistically differ between the two groups as well (10% versus 9%, respectively, OR: 1.26, 95% CI: 0.78-2.03). Subgroup analyses also

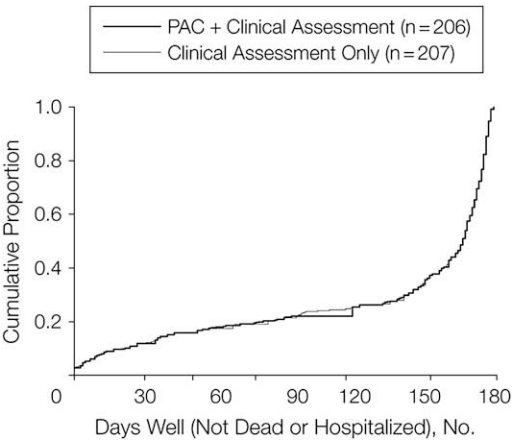

Fig. 2. Cumulative primary end point (days alive and out of hospital) in the ESCAPE trial. Note that the curves overlap for the two treatment groups, pulmonary artery catheter (PAC) plus clinical assessment versus clinical assessment alone. n and NO, number. (*From* Binanay C, Califf RM, Hasselblad V, et al. ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: The ESCAPE Trial. JAMA 2005;294(13):1625–33; with permission.)

generally yielded neutral results when looking at pre-specified factors (**Fig. 3**). Secondary end point analyses revealed a favorable effect on time trade-off for the PAC group, and a trend toward improvement in 6-minute walk during the index hospitalization in the PAC group; however, this trend did not quite reach statistical significance. On the other hand, adverse events were higher in the PAC group (21.9% versus 11.5%, $P = .04$). PAC-related adverse events occurred in nine patients in the PAC group compared with one patient in the clinical assessment group who ended up receiving a PAC later. Most PAC-related adverse events were infection (four patients), with no death linked directly to placement of a PAC.

The ESCAPE trial is a landmark study, being the first large, prospectively randomized, controlled investigation that specifically evaluated the use of PACs in patients with symptomatic, advanced heart failure. As can be readily discerned, the results of the ESCAPE trial do not support the regular use of pulmonary artery catheter in guiding therapy of patients hospitalized with advanced, symptomatic heart failure. The neutral ESCAPE results are in general agreement with prior reports that included heart failure subgroups among their study populations.[7,8]

Several points merit consideration before we finalize conclusions from the ESCAPE trial. First, ESCAPE enrolled patients with symptomatic

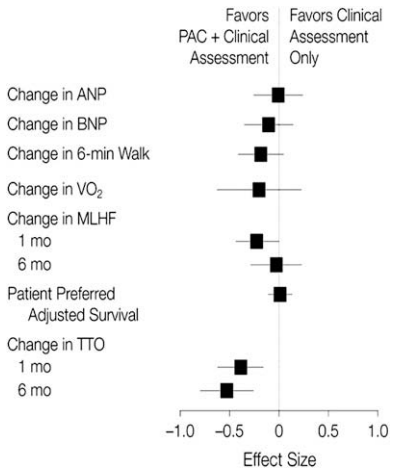

Fig. 3. Changes in secondary end points in the ESCAPE trial. ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; VO_2, peak oxygen consumption; MLHF, Minnesota Living with Heart Failure questionnaire; TTO, time trade-off score. (*From* Binanay C, Califf RM, Hasselblad V, et al. ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: The ESCAPE Trial. JAMA 2005;294: 1625–33; with permission.)

advanced heart failure, for whom clinical management guided by clinical assessment alone was felt reasonably sufficient by experienced heart failure physicians. In other words, patients whose management absolutely required a PAC were actually excluded from the study. Thus, generalization of the ESCAPE trial results to all heart failure patients, regardless of their clinical profile and status should be avoided. Second, the ESCAPE trial did not include patients with cardiogenic shock, or patients being evaluated for mechanical assist devices or urgent heart transplantation. Third, the ESCAPE trial fell short of providing guidelines to choose and guide therapy based on the central hemodynamic data provided by PAC use. The lack of mandated algorithms likely created wide differences among treating physicians in the selection and sequence of therapies (and dosing) for each patient. The effect of this heterogeneous approach on the study outcome is unknown. Finally, the ESCAPE investigators were highly experienced heart failure physicians with outstanding clinical experience and an extraordinary ability to implement their clinical skills in complex patient management. The diminished added benefits of a PAC-guided strategy over therapy guided by their clinical assessment alone may, in part, be the result of a superb performance in the clinical assessment arm (control group). In fact, the rate of PAC-related complications was lower in higher enrollment centers, suggesting the role and impact of skilled physicians in the ESCAPE outcomes.

Could management with PACs actually alter prognosis or is PAC use simply a marker of patients with a worse prognosis? Recently published data from the ESCAPE registry may be informative.[33] The ESCAPE registry enrolled 439 patients excluded from the ESCAPE trial for not meeting the enrollment criteria, and followed them prospectively. Based on the enrolling physician perception, registry patients were classified into three major categories: ''perceived to be too sick,'' ''perceived to be too well,'' and ''unknown.'' The registry patients, in general, were different in their baseline characteristics compared with the trial patients. Hypotension, advanced renal failure, higher usage of intravenous vasoactive medications, and less use of neurohormonal modification therapies (eg, ACE inhibitors, beta blockers) were more common in registry patients. The use of intravenous inotropic agents was twice as high in the registry patients and considered the hallmark of those perceived to be ''too sick'' to be enrolled in the trial. Registry patients were considered to be less congested, but more underperfused than the trial patients, as assessed by the enrolling physicians. However, PAC-derived data revealed a similar overall central hemodynamic profile between the trial and registry patients.

In comparison with the trial patients, registry patients had longer hospitalizations (13 versus 6 days, $P < .001$) and a higher 6-month mortality (34% versus 20%, $P < .001$). Interestingly, the outcome of registry patients who were classified as ''too well to enroll'' was not better than that of other subgroups. In fact, there were no statistical differences between the ''too well to enroll'' and the ''too sick to enroll'' subgroups respectively in length of stay (11 days versus 14 days, $P = .07$) and 6-month mortality (39% versus 33%, $P = .43$). This may be because the perception of ''too well'' was modified by overlooked, important comorbidities.

Analyzing information from the registry database provides us with some insight into the complexity of the ESCAPE trial itself. It is obvious that the ESCAPE trial enrolled patients with lower disease severity and a better prognostic profile than the registry; this fact is confirmed by the considerably higher mortality and longer hospitalizations seen among the registry patients. Another interesting consideration is that the decision of using the PAC itself may have actually singled out patients with high-risk profiles and less favorable outcomes despite similarities in baseline hemodynamics between the trial and the registry patients. Whether PAC use in high-risk patients

has an impact on their clinical outcomes now remains to be seen. In short, it is rather inappropriate to apply the results of the ESCAPE trial to higher-risk patients who require more intense approaches and a rather meticulous selection and adjustment of therapies.

Following the report of the ESCAPE trial, a large meta-analysis of 13 trials (including ESCAPE) involving 5051 critically ill patients was published by Shah and colleagues[34] Most patients (52.8%) in this meta-analysis resided in surgical care units. Because of heterogeneities in therapeutic goals and treatment options among these various trials, a random-effects model was used to compare mortality and number of days spent in the hospital among PAC and non-PAC patients. This meta-analysis showed no significant difference in mortality or days hospitalized between the two groups.

A few other trials merit commentary. The PAC-MAN is a randomized trial from the United Kingdom that investigated PAC use in the critical care setting.[8] There were 1041 patients enrolled between 2001 and 2004; 72% of them were felt to require placement of a PAC to guide vasoactive therapy. Hospital mortality, length of stay in the intensive care units, and the overall hospital length of stay were the same in the PAC and non-PAC groups. However, among the study population, only 11% were managed for heart failure symptoms. Analysis of this small heart failure subgroup showed no differences in study end points between PAC and non-PAC management.

A retrospective look at Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) II and III trials involving 26,437 patients with acute coronary syndromes was published in 2005.[35] PAC use was associated with a higher 30-day mortality in both unadjusted (OR: 8.7, 95% CI: 7.3-1.2) and adjusted (OR: 6.4, 95% CI: 5.4-7.6) analyses.

INDICATIONS FOR PULMONARY ARTERY CATHETERS IN TREATMENT OF HEART FAILURE

One must conclude from the ESCAPE trial that the PAC is no longer a standard component of the management of decompensated heart failure. The American Heart Association/American College of Cardiology (AHA/ACC) guidelines committee in its update of guidelines for management of chronic heart failure lowered the PAC indication to class II B.[36] The guideline states that PAC use might be reasonable to guide therapy in select patients with refractory end-stage heart failure (level of evidence C).

PAC use, however, should be still considered in the management of acute symptomatic heart failure when conventional treatment fails to improve the clinical condition or when volume status cannot be accurately gleaned from clinical assessment alone. PAC can be helpful when management is complicated by renal failure or persistent hypotension to ensure adequate volume status, organ perfusion, and optimal safe dosing of vasoactive drugs.

PAC can still be a useful diagnostic tool in determining the cardiac versus pulmonic etiologies of dyspnea. PAC data can generally identify cardiac origin of pulmonary edema from noncardiac causes, and distinguish between various types of hemodynamic shock when imaging modalities, laboratory data, history, and clinical examination are insufficient. The PAC provides us with the criteria needed to establish the diagnosis of pulmonary arterial hypertension and in selecting drugs, adjusting doses, and performing periodic assessment in the chronic management of the pulmonary hypertension. Finally, the PAC provides the necessary assessment of pulmonary vascular resistance and reactivity of the pulmonary vascular bed in the consideration for cardiac transplantation and/or placement of mechanical supportive devices.

A TRIBUTE TO THE PULMONARY ARTERY CATHETER

Despite the recent decline in general use, the PAC has contributed substantially to the understanding and advancement of basic cardiovascular pathophysiology and clinical cardiovascular medicine. This simple, inexpensive, easy-to-implant and relatively safe device (in experienced hands) allowed two generations of physicians to directly and serially measure central hemodynamic parameters and study the fundamentals of cardiopulmonary physiology and gas exchange in normal and provoked physiologic states (eg, pre- and postexercise), and pre- and postadministration of various cardiovasoactive drugs. PAC augmented our understanding of the hemodynamic effects of various drugs we currently use to treat a considerable number of cardiac and pulmonic diseases in humans. Categorization of drugs, such as preload-reducing and afterload-reducing agents, vasodilators, and positive or negative inotropic drugs, was largely made possible with hemodynamic data provided by PACs; and our understanding of these concepts and their therapeutic role in human disease helped us develop drugs and characterize their function. We learned from the PAC era that the overall acute

hemodynamic responses to vascoactive drugs in heart failure unfortunately do not consistently or directly correspond with their long-term responses and clinical outcomes.[37–40]

Importantly, PACs made us better clinicians by allowing the simultaneous direct bedside assessment of symptoms, physical signs, findings on examination, and the central hemodynamic data and profile.

SUMMARY

The pulmonary artery catheter will likely earn a place in the history of medicine as one of the most useful tools that shaped our understanding and management of various diseases, particularly acute heart failure, decompensated chronic heart failure, and shock conditions. An intense assessment of its general application in nonacute and nonshock decompensated heart failure has now been provided by the ESCAPE trial, a landmark investigation that showed an overall neutral impact of PAC-guided therapy over therapy guided by clinical evaluation and judgment alone. The current guidelines reserve the use of PAC for the management of refractory heart failure and select conditions (eg, pulmonary hypertension, transplant evaluation). In general, the PAC remains a useful instrument in clinical situations when clinical and laboratory assessment alone is insufficient in establishing the diagnosis and pathophysiologic condition, and in guiding effective, safe therapy.

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