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PAC-Man: Game over for the pulmonary artery catheter?

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Expanded Abstract

Citation

Harvey S, Harrison DA, Singer M, Ashcroft J, Jones CM, Elbourne D, Brampton W, Williams D, Young D, Rowan K: Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomized controlled trial. *Lancet* 2005, 366:472-477 [1].

Background

Over the past 30 years, the pulmonary artery catheter (PAC) has become a widely used hemodynamic monitoring device in the management of the critically ill. However, doubts have been raised regarding its benefits and safety. The aim of this study was, therefore, to ascertain whether hospital mortality is reduced in critically ill patients when they are managed with a PAC.

Methods

Design and setting: Prospective, randomized controlled trial of 1041 subjects enrolled in 65 British ICUs.

Subjects and intervention: Patients identified by the treating physician as someone who should be managed using invasive hemodynamic monitoring were randomized to management with (n=519) or without (n=522) a PAC. Subsequent clinical management was at the discretion of the treating clinician. Patients allocated to management with a PAC had the catheter placed as soon as possible after randomization. ICUs were stratified *a priori* depending on whether they wished to have the option of using an alternative cardiac output-monitoring device (other than CVP monitoring and clinical examination) in control patients.

Outcomes: The primary end-point of the study was hospital mortality.

Results

After exclusion of 27 patients due to lack of consent after randomization, there were 1014 subjects eligible for analysis. No difference in hospital mortality between subjects managed with or without a PAC was noted (68% [346 of 506] vs. 66% [333 of 507], p=0.39; adjusted hazard ratio 1.09, 95% CI 0.94–1.27). Complications associated with insertion of a PAC were noted in 46 of 486 (10%) individuals in whom the device was placed but none were considered fatal. Complications were not recorded in the control arm, precluding conclusions regarding the relative safety of the PAC. Of patients randomized to receive either a PAC or no monitor of cardiac output, mortality was 71% [75 of 105] vs. 66% [71 of 107], p=0.46, respectively (adjusted hazard ratio 1.21, 95% CI 0.87-1.68). Of patients randomized in ICUs allowing the possibility of an alternative monitor of cardiac output, mortality was 68% [271 of 401] vs. 66% [262 of 400], p=0.55, respectively (adjusted hazard ratio 1.06, 95% CI 0.90-1.26).

Conclusion

The authors conclude their findings indicate no clear evidence of benefit or harm in managing critically ill patients with a PAC and suggest efficacy studies that couple PAC use to explicit management protocols are necessary.

Commentary

While knowledge of PAC-derived data has obvious appeal, concern emerged in the early 1990s that PAC use might be associated with higher mortality. An attempt to conduct a randomized controlled trial failed in 1991 when only thirty-three of 148 potentially eligible patients were randomized [2]. Subsequently, a large retrospective study by Connors et al. concluded PAC use was associated with increased 30-day mortality (odds ratio 1.24) [3]. This study was a

substantial improvement on prior non-randomized studies. Moreover, this paper's main conclusion was that the PAC had been shown to be of such questionable utility that there is sufficient equipoise for a randomized controlled trial. A controversial accompanying editorial called for a moratorium on PAC use in the absence of such data [4]. In response, there have been a number of large randomized trials of the PAC in a variety of patient populations. The PAC was shown to be without benefit when the device was used to guide goal directed perioperative care or care for congestive heart failure [5,6], though most patients in the PAC arm of the perioperative care study failed to achieve the specified physiological goals in the pre- or intra-operative period [6]. Prior to PAC-Man, only two randomized controlled trials of PAC use in a general ICU population had been published. One of these studies was markedly underpowered [7], while a recent French study showed the PAC had no effect on mortality [8]. The power of the French study was also less than planned due to slower than expected enrollment, such that there was eventually only 78% power to detect a 10% absolute difference in mortality.

The current study is the largest and best-powered trial thus far in a general intensive care population and has yet again failed to demonstrate any benefit with PAC use. The study had an 82% power to detect a 10% change in mortality. While the authors present most of their results as a comparison of PAC versus no PAC, this approach ignores the fact that essentially two studies were performed: one of PAC vs. no cardiac output (CO) monitor (stratum A), and the other of PAC vs. an alternate CO monitor (stratum B). Combining the studies answers the question "do PACs provide any benefit over conventional practice, whatever that is?" but not "are PACs superior to no monitor of CO?" or "are PACs superior to less invasive monitors of CO?." Based on pilot studies, the authors expected half of the units to opt for each stratum, which (with 650 patients in each group) would have given a 62% power to detect a change in hospital mortality in each group (Harvey, personal communication). As it turned out, the perceived utility of CO monitoring by at least some means was such that 79% of patients were enrolled in units that had elected to join Stratum B. Though an analysis comparing outcome of patients who actually received an alternate CO monitor to those in the PAC group was not presented, this was presumably adequately powered. A post-hoc analysis is currently in preparation, based on the observation that mortality in all three groups (PAC, no PAC, and no PAC +/- some other CO monitor) was very similar, suggesting that either few patients in the no PAC +/- other CO monitor group actually received a CO monitor, or that no monitor of CO output had an impact on mortality. This post-hoc analysis should hopefully further delineate the utility of CO monitoring by any means (Harvey, personal communication).

PAC-Man was an *effectiveness*, or pragmatic, study of the PAC in actual practice, and so did not rely on treatment directed by protocol. Because the PAC is already disseminated, such a study is warranted. However, it is possible that the lack of benefit was because clinicians did not act on PAC data "correctly." Of note, however, there was no outcome difference in ICUs with differing prior PAC experience. Another trial which has just completed enrollment but is not yet analyzed, the NIH-funded Fluid and Catheter Treatment Trial (FACTT), represents an attempt to conduct an *efficacy* trial where the interpretation and subsequent decisions were entrained within tightly administered protocols. This study has generated considerable controversy even before its completion, because of disagreement over what constitutes a safe approach to fluid management in the critically ill [9]. If FACTT is positive, it will provide clear direction regarding PAC use and the best associated management decisions. However, a negative trial may simply stir on-going debate about what constitutes the "correct" use and interpretation of PAC-derived data.

One interesting observation from PAC-Man was the decision by the majority of ICUs to participate in stratum B. In other words, clinicians in most of the ICUs felt that some attempt to monitor central hemodynamics was required, even though the alternative monitoring devices employed have undergone even less scrutiny in large randomized trials than the PAC. The wide dissemination of the PAC before rigorous evaluation has made subsequent assessment of its value very difficult, with lack of equipoise hampering randomization and numerous opinions regarding how the PAC should be used complicating study design. Determining the worth of new monitoring devices may prove equally difficult given the ongoing desire to adopt them before adequate evaluation has been completed.

There have now been at least six randomized controlled trials of PAC use in general or specialist intensive care, none of which has shown the PAC to be of harm or benefit. Nonetheless, PAC use continues, with no standardized agreement about what represents appropriate use. As with the thermometer, which assigns a number to a clinical condition relatively easily assessed by clinical examination, the benefit may be to the physician (in terms of ease of management) rather than the patient (in terms of outcome). While an effect on mortality has not been seen in these PAC trials, complications have been reported. For example, there was a higher rate of pulmonary embolism in a prior Canadian study [6]. Furthermore, all central lines are associated with a variety of complications related to placement and infection, some of which are life-threatening, even if rare.

Recommendation

Given the difficulty demonstrating patient benefit, we recommend that the clinician weigh carefully the perceived benefits, which may be largely intangible, against the small, but non-zero, risk of harm to the patient. Until an alternative is found superior, the decision to insert a PAC must be

made on a case-by-case basis. Use of the PAC should be much more selective than in the past, and in many instances should perhaps also involve discussion with the patient or family. In the meantime, the safety and efficacy of alternative monitors of cardiac output must be tested, if the mistakes associated with the widespread adoption of the PAC are to be avoided.

Competing interests

MCR declares no competing interests. DCA is funded by the US National Institutes of Health to study the cost-effectiveness of the PAC (EA-PAC R01 HS011620).

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