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Arterial Lines in the ICU
A Call for Rigorous Controlled Trials

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The appropriate justification for using a diagnostic or therapeutic intervention is that it provides benefit to patients, society, or both. For decades, indwelling arterial catheters have been used very commonly in patients in the ICU, despite a complete absence of data addressing whether they confer any such benefits. Both of the main uses of arterial catheters, BP monitoring and blood sampling for laboratory testing, can be done without these invasive devices. Prominent among complications of arterial catheters are bloodstream infections and arterial thrombosis. To my knowledge, only a single observational study has assessed a patient-centered outcome related to arterial catheter use, and it found no evidence that they reduce hospital mortality in any patient subgroup. Given the potential dangers, widespread use, and uncertainty about consequences of arterial catheter use in ICUs, equipoise exists and randomized trials are needed. Multiple studies in different, well-characterized, patient subgroups are needed to clarify whether arterial catheters influence outcomes. These studies should assess the range of relevant outcomes, including mortality, medical resource use, patient comfort, complications, and costs. CHEST 2014; 146(5):1155-1158

ABBREVIATIONS: AC = arterial catheter; PAC = pulmonary artery catheter

The only appropriate justification for using a diagnostic or therapeutic intervention is that it provides benefit to patients, society, or both. In the context of ICU care, the patient-centered benefit that receives the most attention is survival; however, many other outcomes are relevant to patients. These include rates of complications, care-related pain and suffering, subsequent physical and cognitive functioning, and quality of life.[1] Even if an intervention provides no benefit to patients, it could benefit society in the form of lower costs, producing better cost-effectiveness of care. Because every intervention has real costs and real risks, interventions without such benefits should not be routinely used.

Despite decades of effectiveness research, there are numerous interventions used in medical practice for which there are no data directly addressing how they influence relevant outcomes. While physiologic rationale, anecdotes, and other forms of empirical reasoning have formed the basis for many of the interventions used in clinical practice, these are fraught with dangers. Our

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physiologic understanding is imperfect. Anecdotes, or the fact that an intervention has been used for many years and, therefore, "must" be of benefit, are not scientific arguments.[2] While such arguments go back more than a century,[3] there are numerous modern examples of interventions that made sense, yet when studied were proven to be of no benefit, or even harmful. ICU therapies in this category include nesiritide in severe congestive heart failure,[4] extracranial-intracranial bypass for ischemic stroke,[5] hyperventilation for traumatic brain injury,[6] low-dose dopamine in early renal dysfunction,[7] and starches for volume resuscitation.[8] Even though data can be imperfect, and we will always be limited by the best data available to us, high-quality data trump such reasoning.

The best example in the realm of physiologic monitoring is pulmonary artery catheters (PACs). The rationale for PAC use is strong: Studies have consistently shown that expert clinicians cannot accurately estimate the parameters measured by PACs.[9-12] Although PAC use has risks and there was a lack of evidence for any benefit from this device,[13] by the 1990s millions were used yearly.[14] Now, after 14 randomized trials, no subgroup of critically ill patients has been identified for whom PAC use improves clinically relevant outcomes.[15,16]

With this background, we now discuss the indwelling arterial catheter (AC), a technology that is routinely and very extensively used in ICUs—without evidence about its effect on relevant outcomes. Approximately one-third of all patients in the ICU in the United States receive an AC, with even higher use in some subgroups.[17] This amounts to almost 2 million patients receiving ACs yearly,[18] and, with replacements and reinsertions, the number of AC procedures and catheters is likely much higher. Use of AC appears to be even more common in Canada.[19]

ACs are used mainly for BP monitoring, and to facilitate diagnostic blood testing, including arterial blood gas analysis. However, these goals do not require an AC. BP can be monitored noninvasively. Blood drawn for laboratory testing can be obtained by intermittent arterial puncture or phlebotomy.

A commonly held, but erroneous, belief is that systolic and diastolic BP measurements from ACs are "correct," while noninvasive values are a problematic surrogate. It is true that automated noninvasive BP measurements are prone to various artifacts,[20] and that values can occasionally differ substantially between the two methods.[21-24] On the other hand, virtually everything that is known about the epidemiology of BP, and the information we obtain about a given person's usual, outpatient BP, derive from noninvasive measurements. Furthermore, in vivo and in vitro studies have identified a variety of artifacts in AC-derived BP measurements that can result in values that are too high or too low.[20,25-27] With both types of BP measurements prone to inaccuracies, the question of true importance is whether patient management with one vs the other modality results in differences in relevant outcomes. To my knowledge only two human studies, both observational, have sought to address this question. In a single-center study of 150 patients, Lakhal et al[24] found that automated noninvasive BP identified hypotension, defined as AC-derived mean arterial pressure < 65 mm Hg, with a sensitivity and specificity of 95%. The only study that has addressed a patient-centered outcome is a propensity-matched analysis of hospital mortality performed on the Project IMPACT database by Gershengorn et al.[28] That study found no difference in mortality in the primary cohort of medical-type patients who were mechanically ventilated, or eight of nine secondary cohorts; however, among almost 11,000 patients needing vasopressors for shock, mortality was higher in patients who received an AC (OR, 1.08; $P = .008$).[28] Regarding ACs to facilitate laboratory blood testing, their presence is associated with excessive testing,[29] even independent of the test results.[30] Not only does this increase costs, but excessive phlebotomy promotes anemia and consequent blood transfusion.[31,32] In general, more testing has not been associated with improved clinical outcomes.[33,34]

The direct complications related to ACs include, but are not limited to, infection and arterial thrombosis.[35,36] Although AC devices look like peripheral IV catheters, the rate of bloodstream infections associated with them is 2.5-fold higher.[37,38] The poor recognition of this danger may result from poor concordance between AC tip cultures vs blood cultures drawn through the AC, and to the finding that infected ACs rarely appear infected to the naked eye.[39] Thrombosis related to ACs is not rare, though most of the consequent ischemia is temporary.[35,40-43]

In the face of these risks, why then are ACs used so ubiquitously? Intensivists trained in centers where AC use is routine often never critically question the teaching that critically ill patients "require" ACs. While it seems plausible that measuring BP every 100 milliseconds with an AC would lead to better outcomes for patients with shock on vasoactive drugs, the only study that has addressed this question, to my knowledge, has not found it to be true.[28] Another common rationale for AC

use is to avoid patient discomfort from percutaneous phlebotomy, or frequent BP cuff inflations. And while these are legitimate concerns about patient-centered outcomes, this calculus must include the discomfort of AC insertion, and must balance discomfort with the risks to life and limb related to ACs.

The widespread use of ACs without evidence for benefit is likely due, in part, to the fact that clinical practice patterns are often based on "expert opinion, historical practice, and blind acceptance, rather than on an adequate evidence base".[44] Five years ago, after I gave a lecture on ACs at a national meeting, a senior intensivist stated that even if ACs confer no benefit to patients or to society, they are valuable because they can make physicians feel more comfortable. Such arguments are difficult to countenance. The medical system exists to improve the health of patients and of society. Unless the intervention is free and carries no potential risks, it is a slippery slope to justify it based on comfort or convenience of the caregivers.

Given the potential dangers, widespread use, and uncertainty about consequences of AC use, high-quality, randomized trials are needed. There is equipoise for this question. As summarized previously, these devices carry risks. In reminding us about the Hippocratic imperative, Singer and Glynne[44] have cautioned us that "superficially attractive, short-term benefits may camouflage underlying tendency to cause harm" and reminded us that the "major advances of intensive care medicine in the last 20 years have been related more to the recognition and removal of harmful practices rather than to any novel pharmacological or mechanical interventions."[44] Wide variation in AC utilization represents the uncertainty.[17,45] The evolution of research on PACs, previously discussed, is instructive. Cautions about placing ACs was a finalist among critical care expert opinion recommendations in the Choosing Wisely Campaign of the American Board of Internal Medicine.[46] The sole observational study on clinically relevant outcomes from AC use did not show a benefit.[28]

Just as for PACs, multiple studies in different, well-characterized, patient subgroups will be needed to clarify whether ACs influence outcomes. These studies should assess the range of relevant outcomes, including mortality, medical resource use, patient comfort, complications, and costs. Of course, even if no patient subgroup is found to benefit, these devices will still be appropriate in rare patients when no other modality allows for obtaining needed information, such as when meaningful noninvasive BP measurements cannot be obtained.

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Original Investigation

Association Between Arterial Catheter Use and Hospital Mortality in Intensive Care Units

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IMPORTANCE Arterial catheters are used frequently in intensive care units (ICUs). Clinical effectiveness and adverse events associated with the use of the catheters have not been formally evaluated in clinical studies.

OBJECTIVE To determine whether an association exists between arterial catheter use and hospital mortality in ICU patients.

DESIGN, SETTING, AND PARTICIPANTS Propensity-matched cohort analysis of data in the Project IMPACT database, from 2001 to 2008. A total of 139 ICUs in the United States were included. Participants were ICU patients 18 years or older.

EXPOSURE Arterial catheter use.

MAIN OUTCOMES AND MEASURES Our main outcome was hospital mortality. We assessed a primary cohort of medical patients requiring mechanical ventilation and 9 secondary cohorts. We used propensity score–matched pairs as the primary analytic strategy. Sensitivity analyses included 4 alternative methods of comparison in the primary cohort: multivariate modeling without propensity adjustment, mixed-effects multivariate logistic regression without propensity adjustment, multivariate modeling with propensity adjustment, and stratification based on propensity quintiles.

RESULTS Our primary cohort consisted of 60 975 patients; 24 126 of these patients (39.6%) had an arterial catheter in place during their ICU stay, and analyses were based on 13 603 propensity score–matched pairs. We found no association between arterial catheter use and hospital mortality in medical patients requiring mechanical ventilation in the primary analysis (odds ratio [OR], 0.98; 95% CI, 0.93-1.03; $P = .40$) or the 4 sensitivity analyses ($P \geq .58$ for all). In 8 of 9 secondary cohorts we were unable to detect an association between arterial catheter use and hospital mortality. In the cohort of patients receiving vasopressors, arterial catheter use was associated with an increased odds of death (OR, 1.08; 95% CI, 1.02-1.14; $P = .008$).

CONCLUSIONS AND RELEVANCE In this propensity-matched cohort analysis, arterial catheters were not associated with improvements in hospital mortality in medical ICU patients requiring mechanical ventilation. Given the costs and potential harms associated with invasive catheters, randomized clinical trials are needed to further evaluate the usefulness of these frequently used devices.

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The use of diagnostic and therapeutic interventions in modern medical practice should ideally be supported by evidence demonstrating net benefit. However, many interventions in use over long intervals are assumed to be beneficial without data to support them.[1-3]

Arterial catheterization is a commonly used intervention in intensive care units (ICUs) worldwide. In the United States, 36% of all patients receive an arterial catheter (AC) during their ICU stay.[4] Arterial catheters are inserted to facilitate diagnostic phlebotomy, augment hemodynamic monitoring, or monitor arterial blood gases.[5-8] However, ACs are associated with measurable risks, such as limb ischemia,[9] pseudoaneursyms,[10,11] and catheter infections,[12-18] as well as costs for insertion and maintenance.[19,20] Significant variability in AC use exists across ICUs in the United States that is more attributable to an individual ICU than to patient-specific characteristics.[4] Practice variability may stem partially from a paucity of data regarding the effect of ACs on patient-centered outcomes in the critically ill population. We, therefore, conducted a cohort study to examine the association between AC use and clinical outcomes in critically ill patients. We hypothesized that we would observe no association between AC use and hospital mortality.

Methods

We performed an analysis of all adults (≥18 years) admitted from January 1, 2001, through December 31, 2008, to ICUs in the United States participating in Project IMPACT (Cerner Corporation).[21] Institutional review board exemption was obtained from Albert Einstein College of Medicine. Project IMPACT was developed to provide regular performance audits and feedback to participating ICUs. Participation was voluntary and ICUs paid for the service. Information was collected by on-site data collectors who were certified to ensure standardization in data definitions and entry. Hospitals participating in Project IMPACT tended to be larger and more urban than general-population hospitals, but were diverse in size and location. Data were either from consecutive admissions to each ICU or a random sample of admissions. Sites using the latter method collected information on 50% or 75% of all patients; the percentage was determined quarterly before data collection commenced.

We included only the patient's initial ICU admission for a given hospital stay. Available data included patient demographics (age, sex, race/ethnicity, and insurance provider), severity of illness as described by the Mortality Probability Model III–predicted hospital mortality at ICU admission (MPM_0-III),[22] preference for cardiopulmonary resuscitation at ICU admission and during the ICU stay, Acute Physiology and Chronic Health Evaluation II (APACHE II) diagnostic category,[23] location before ICU arrival, need for cardiopulmonary resuscitation within 24 hours before ICU arrival, vital signs on ICU admission (heart rate >150 beats/min, systolic blood pressure <90 mm Hg, fraction of inspired oxygen required >50%), patient categorization (medical, emergency surgery, or elective surgery), comorbidities, year of ICU admission, and number of organs failing during the ICU admission. Comorbidities were defined by a list of 16 chronic conditions used for severity-of-illness score calculations. Explicit definitions for organ failure were provided by Project IMPACT.[24] Data on interventions included the use of invasive mechanical ventilation, the use of intravascular catheters (arterial, central venous, and/or pulmonary artery), and vasopressor administration by continuous intravenous infusion (epinephrine, norepinephrine, dopamine, phenylephrine, and/or vasopressin). Intensive care units and hospitals were characterized according to ICU type, ICU model (closed vs open), mean nurse to patient ratio, and hospital organization (city, state, or federal government; community; or academic).

Reporting of data on intravascular catheter use, including ACs, was mandatory in Project IMPACT. Patients were considered to have had an intravascular catheter if it was in place for any portion of the ICU stay, regardless of whether it was placed in the ICU or before ICU arrival. Arterial catheters were included if they were placed in the dorsalis pedis, radial, axial, femoral, or brachial arteries; documentation of the site was not required and was not consistently available.

Our primary outcome was hospital mortality. Other patient-centered outcomes included days requiring vasopressor support, days of mechanical ventilation, and ICU length of stay. We additionally evaluated the rate of packed red blood cell (PRBC) transfusions. The PRBC transfusions were hypothesized to be a negative consequence of AC use because of additional phlebotomy and/or bleeding at the catheter site.[25] We also conducted falsification analyses by testing for associations between AC use and 4 other interventions that were not presupposed to be related to AC use: platelet transfusions, paracentesis, lumbar puncture, and transesophageal echocardiography.

Cohorts

To reduce patient-level heterogeneity, for our primary analysis we assessed a primary cohort of medical patients (no surgery within the 7 days before ICU admission) who arrived in the ICU from any location other than the operating room or postanesthesia care unit and who required mechanical ventilation at any point during their ICU stay. Prior work established that there was large variability in the use of ACs in this population.[4] To evaluate the generalizability of our findings, we repeated the main analyses on 9 secondary cohorts: medical patients requiring mechanical ventilation in the (1) lowest, (2) middle, and (3) highest tertiles of MPM_0-III; (4) medical patients requiring mechanical ventilation admitted to mixed medical-surgical ICUs in which AC use for surgical patients was within the 25th to 75th percentile of all mixed ICU use (to address issues of possible AC documentation errors); (5) all ICU patients (ie, not limited to medical patients or patients requiring mechanical ventilation); (6) all patients admitted to mixed medical-surgical ICUs; (7) all patients requiring vasopressors at any point during their ICU stay; (8) all patients with septic shock (as defined by the sepsis APACHE II diagnostic category plus the need for vasopressors at any point during the ICU stay); and (9) surgical patients (underwent surgery within the 7 days before ICU admission and were admitted to the ICU from the operating room or postanesthesia care unit) who re-

quired mechanical ventilation at any point during their ICU stay. Owing to the high rates of ACs placed for intraoperative purposes, for the surgical mechanically ventilated cohort, we defined AC use in the ICU as either placement in the ICU or placement before arrival in the ICU with removal more than 1 day after arrival in the ICU. In this analysis, all patients who died within 24 hours of ICU admission were excluded and comparison was made with surgical patients requiring mechanical ventilation who never had an AC.

Statistical Analysis

The statistical plan was determined a priori. Additional analyses were conducted as requested upon manuscript review.

Association Between AC Use and Hospital Mortality

Five distinct analytic approaches were taken to assess the relationship between AC use and hospital mortality: (1) propensity matching (our primary analysis), (2) multivariate logistic regression without propensity adjustment, (3) mixed-effects multivariate regression without propensity adjustment, (4) multivariate logistic regression with propensity adjustment, and (5) stratification based on propensity quintiles.[26-28] Only the primary analysis (propensity matching) was performed for the secondary cohorts.

Propensity Score Calculation | A propensity score is a probabilistic measure that reflects the propensity of a patient, based on other characteristics, to receive an AC. This score is not a marker of whether particular patients received an AC but rather whether they were likely to do so given their characteristics. For each cohort, the propensity to receive an AC was calculated using multivariate logistic regression with AC use as the dependent variable and all available patient characteristics as the independent variables.[29-31] Clustering of patients within individual ICUs, which we a priori assumed would have a significant effect on the use of ACs,[4] was modeled by including the individual ICU as a fixed effect in the model.[32,33] To allow for nonlinear relationships, continuous variables were included in the model as 4-knot cubic splines.[34] The success of the propensity score is determined by its ability to balance independent covariates between the patients who received ACs and those who did not. This covariate balance was assessed using standard mean differences.[35]

Propensity-Matched Analysis (Primary Analysis) Propensity matching is a technique in which quasi-case/control pairs are produced from a retrospective cohort. For our cohorts, patients who received an AC were matched to patients who did not receive an AC but had a similar propensity to do so. Matching was performed, after randomly ordering patients, using the psmatch2 algorithm[36] in Stata, version 11.1 (StataCorp), with 1 to 1 nearest-neighbor matching without replacement and with maximal caliper distance of 25% of the SD of all propensity scores. In addition, exact matching was used for each covariate for which the propensity score did not achieve appropriate balance.

Standard summary statistics were used to compare the baseline patient-, ICU-, and hospital-level characteristics between groups of propensity-matched cases and controls. The odds of hospital mortality were compared between the 2 matched groups using χ^2 statistics.

Multivariable Logistic Regression Without Propensity Adjustment We used multivariable logistic regression to assess the association between hospital mortality and AC use after adjusting for all covariates. The individual ICU was included as a fixed effect.

Mixed-Effects Multivariable Logistic Regression Without Propensity Adjustment We used mixed-effects multivariable logistic regression to assess the association between hospital mortality and AC use after adjusting for all covariates. All patient-level independent variables were entered into the model as fixed effects; the individual ICU was included as a random effect.

Multivariable Logistic Regression With Propensity Adjustment The addition of propensity adjustment to a multivariate model has been advocated as a method to further adjust for confounders that may be related to the independent and the dependent variables.[37] In this analysis, we performed the same multivariate logistic regression outlined in the previous section with the addition of the propensity score as an independent variable to calculate the adjusted odds of hospital mortality associated with AC use.

Stratification Based on Propensity Quintiles Stratification based on propensity percentiles is a method for comparing outcomes among patients with a similar likelihood of receiving the intervention (eg, AC use). Stratification into quintiles is commonly used because it is adequate to remove 90% of all bias.[38] We divided our primary cohort into quintiles of propensity score and evaluated the odds of hospital mortality associated with AC use within each quintile. Combination of these odds ratios (ORs) into a single OR across the entire cohort was done using the Mantel-Haenszel method.[39]

Sensitivity Analysis to Address Potential Immortal Time Bias | Immortality bias arises when patients in a retrospective analysis who are exposed to the intervention of interest have their exposure at varying times after the start of the study period.[40,41] These individuals must have survived until their intervention, making them "immortal" in the time preceding it. Thus, exposed patients are biased toward better survival outcomes than their nonexposed counterparts who do not experience this immortal time. To address this potential bias, we conducted a sensitivity analysis of patients in the primary cohort who survived for at least 2 days, comparing matched pairs of those who received an AC during their first ICU day vs those who never received an AC.

Association Between AC Use and Other Patient-Centered Outcomes

Using the primary analytic strategy (propensity matching), we evaluated the association between AC use with vasopressor days (the total number of ICU days on which the patient received ≥1 vasopressor agents), mechanical ventilation duration (the first episode as well as the total number of days requiring mechanical ventilation), and ICU length of stay. Because

these outcomes are also subject to immortal time bias, we conducted these analyses for the primary cohort of medical patients requiring mechanical ventilation as well as the subset of these patients who were in the ICU on day 2 and with or without an AC on day 1.

Association Between AC Use and Other Interventions

We assessed the association between AC use and PRBC transfusions using propensity matching applied to the primary cohort of medical patients requiring mechanical ventilation. To exclude patients who received transfusions for treatment of gross hemorrhage, we restricted transfusion outcomes to patients who received at most 2 U of PRBCs on any given day. Because we assessed the number of PRBCs transfused per day, we excluded patients in whom ICU length of stay was not recorded. A total of 3481 patients (5.7% of the primary cohort) were excluded. After these exclusions, we performed the propensity scoring and matching. For falsification analyses,[42] we also evaluated 4 interventions that we hypothesized would not be associated with AC use: platelet transfusion, paracentesis, lumbar puncture, and transesophageal echocardiography. Because many patients received none of these interventions, comparisons used zero-inflated negative binomial regression modeling on the matched patients, with the ICU length of stay as an offset and the AC status being the sole independent variable; in such a model, the exponentiated coefficient represents the rate ratio of units of the intervention per ICU day associated with having had an AC.[43] Database management and statistical analyses were performed using Excel (Microsoft) and Stata, version 11.1 (StataCorp).

Results

Characteristics of Matched Cohort

Our primary cohort consisted of 60 975 medical patients who required mechanical ventilation in 139 ICUs in 119 hospitals; 24 126 (39.6%) of the patients had an AC (eTable 1 in the Supplement). Propensity score matching yielded 13 603 pairs of patients who did not have an AC and patients who did have an AC (**Table 1** and eTable 2 and eTable 3 in the Supplement). The initial propensity score model for the primary cohort achieved balance on all but 5 covariates (pulmonary artery catheter use, central venous catheter use, vasopressor use, initial fraction of inspired oxygen greater than 50%, and mechanical ventilation on ICU admission); these 5 factors were exactly matched upon to make the final matches. All patient-level characteristics were statistically balanced after matching with the exception of minor differences in age (mean [SD], 59.0 [18.3] in the no-AC group vs 58.2 [18.4] in the AC group) and primary insurance (Medicare 48.5% vs 46.6%, respectively). Two ICU/hospital-level characteristics differed, again by small amounts, between the 2 groups: ICU type ($P < .001$) and hospital organization ($P = .003$). The matched cohort was 78.4% white and 56.6% male with a mean (SD) MPM_0-III–predicted hospital mortality of 26.9% (23.6%). On ICU admission, 63.5% of the patients were receiving mechanical ventilation; at some point during their ICU stay, 44.5% required vasopressors, 72.8% had a central venous catheter, and 5.3% had a pulmonary artery catheter. Approximately 53% of the patients were admitted to mixed medical-surgical ICUs.

Hospital Mortality

Using propensity matching, we demonstrated no association between AC use and hospital mortality in the primary cohort of medical patients requiring mechanical ventilation: the OR for hospital mortality associated with having an AC was 0.98 (95% CI, 0.93-1.03) (**Table 2**). The hospital mortality was 35.5% for patients who received an AC and 36.0% for patients who did not. Each of the 4 alternative statistical analyses yielded similar findings, as did the sensitivity analysis focused on minimizing immortal time bias (eTable 4 in the Supplement).

In 8 of the 9 secondary cohorts, propensity-matched analysis revealed no association between AC use and mortality (**Figure**). In patients requiring vasopressors, the odds of death was increased in patients who received an AC (OR, 1.08; 95% CI, 1.02-1.14; $P = .008$).

Secondary Patient-Centered Outcomes

Days requiring vasopressors, duration of mechanical ventilation, and ICU length of stay were all greater for patients who received ACs (eTable 5 in the Supplement). Restriction to the subset of patients who had ACs on day 1 and survived at least until day 2 did not alter the results.

Association With Other Interventions

In the primary cohort of medical patients receiving mechanical ventilation, we found no association between PRBC transfusions and AC use (rate ratio, 0.99; 95% CI, 0.82-1.19; $P = .91$) (**Table 3**). Similarly, we found no association between platelet transfusion, paracentesis, lumbar puncture, or transesophageal echocardiography and AC use.

Discussion

In this propensity-matched cohort analysis, we found no association between AC use and hospital mortality in medical ICU patients who require mechanical ventilation. Our results were robust through 4 different modeling methods. Similarly, in the analyses of 8 of 9 secondary cohorts, we found no association between AC use and hospital mortality. In one secondary cohort (patients requiring vasopressors), AC use was associated with an 8% increase in the odds of death.

We found no other study that reports clinically meaningful outcomes associated with AC use. There is a growing number of studies, however, evaluating the impact of other monitoring devices that are generally made available with less scrutiny than is required for pharmacotherapeutics.[44] First, pulmonary artery catheters, once commonly used in the ICU, are being used less frequently.[45-47] Although replacement with noninvasive monitors likely accounts for some of this decline, it likely is also because of the growing evidence that these catheters do not improve outcomes.[48-52] Second, a

Table 1. Baseline Characteristics of Propensity-Matched Pairs of Medical Patients Requiring Mechanical Ventilation

Characteristic	Catheter, No. (%)		*P* Value
	No Arterial	Arterial	
Patient-level factors			
No. of patients	13 603	13 603	
Age, mean (SD), y	59.0 (18.3)	58.2 (18.4)	<.001
Race/ethnicity			
White	10 692 (78.6)	10 646 (78.3)	.79
Black	1961 (14.4)	1991 (14.6)	
Other	950 (7.0)	966 (7.1)	
Male sex	7687 (56.5)	7709 (56.7)	.78
MPM_0-III score, mean (SD)	0.27 (0.24)	0.27 (0.24)	.34
Primary insurance			
Private	3627 (26.7)	3739 (27.5)	.009
Medicare	6591 (48.5)	6345 (46.6)	
Medicaid	1478 (10.9)	1448 (10.6)	
Self-pay	1453 (10.7)	1566 (11.5)	
Other	454 (3.3)	505 (3.7)	
Chronic health conditions[a]			≥.15
APACHE II acute diagnostic category[a]			.70
Location prior to ICU admission			
Emergency department	8050 (59.2)	8121 (59.7)	.38
Other	5553 (40.8)	5482 (40.3)	
Heart rate >150 beats/min in first 24 h in ICU	635 (4.7)	612 (4.5)	.51
Systolic blood pressure <90 mm Hg in first 24 h in ICU	4439 (32.6)	4421 (32.5)	.82
Fraction of inspired oxygen >50% in first 24 h in ICU[b]	8504 (62.5)	8504 (62.5)	>.99
Invasive mechanical ventilation at time of ICU admission[b]	8634 (63.5)	8634 (63.5)	>.99
CPR within 24 h prior to ICU arrival	1311 (9.6)	1261 (9.3)	.30
Do-not-resuscitate order in place			
At ICU admission	26 (0.2)	27 (0.2)	.89
During ICU stay	831 (6.1)	811 (6.0)	.61
ICU admission, y			
2001	895 (6.6)	891 (6.6)	.98
2002	1740 (12.8)	1697 (12.5)	
2003	1883 (13.8)	1907 (14.0)	
2004	1961 (14.4)	1972 (14.5)	
2005	1987 (14.6)	2012 (14.8)	
2006	1929 (14.2)	1929 (14.2)	
2007	1767 (13.0)	1790 (13.2)	
2008	1441 (10.6)	1405 (10.3)	
No. of organ systems failing during ICU stay			
0	7427 (54.6)	7508 (55.2)	.83
1	2740 (20.1)	2663 (19.6)	
2	1626 (12.0)	1592 (11.7)	
3	968 (7.1)	961 (7.1)	
4	517 (3.8)	522 (3.8)	
5	231 (1.7)	250 (1.8)	
6	88 (0.6)	100 (0.7)	
7	6 (0.04)	7 (0.1)	
Vasopressors used[b]	6054 (44.5)	6054 (44.5)	>.99
Central venous catheter used[b]	9899 (72.8)	9899 (72.8)	>.99
Pulmonary artery catheter used[b]	724 (5.3)	724 (5.3)	>.99

(continued)

Table 1. Baseline Characteristics of Propensity-Matched Pairs of Medical Patients Requiring Mechanical Ventilation (continued)

Characteristic	Catheter, No. (%)		*P* Value
	No Arterial	Arterial	
ICU/hospital-level factors			
ICU type			
MICU/SICU	7288 (53.6)	7221 (53.1)	.02
CCU	119 (0.9)	109 (0.8)	
MICU	1521 (11.2)	1437 (10.6)	
MICU/CCU	633 (4.7)	636 (4.7)	
MICU/CCU/SICU	1690 (12.4)	1626 (12.0)	
SICU	613 (4.5)	645 (4.7)	
SICU/trauma	1222 (9.0)	1318 (9.7)	
Trauma	517 (3.8)	611 (4.5)	
ICU model			
Open	7901 (58.1)	7891 (58.0)	.90
Closed	5702 (41.9)	5712 (42.0)	
Nursing ratio			
1:1	120 (0.9)	123 (0.9)	.70
1:2	13 091 (96.2)	13 103 (96.3)	
1:3	101 (0.7)	85 (0.6)	
1:4	291 (2.1)	292 (2.1)	
Hospital organization			
City, state, federal government	9034 (66.4)	8814 (64.8)	.003
Community	580 (4.3)	548 (4.0)	
Academic	3989 (29.3)	4241 (31.2)	

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation, II; CCU, coronary care ICU; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; MICU, medical ICU; MPM_0-III, Mortality Probability Admission Model–predicted hospital mortality at ICU admission, III; SICU, surgical ICU.

[a] Detailed breakdown of chronic health conditions and APACHE II acute diagnostic categories presented in eTable 2 in the Supplement.

[b] Fraction of inspired oxygen >50% in first 24 hours in the ICU, invasive mechanical ventilation at time of ICU admission, vasopressors used, central venous catheter used, and pulmonary artery catheter used were matched for exactly.

Table 2. ORs for Hospital Mortality Associated With Arterial Catheter Use for Medical Patients Requiring Mechanical Ventilation

Characteristic	OR (95% CI)	*P* Value
Propensity-matched sample	0.98 (0.93-1.03)	.40
Alternative analyses[a]		
Multivariate logistic regression without propensity adjustment	0.99 (0.92-1.06)	.77
Mixed-effects multivariate logistic regression without propensity adjustment	0.98 (0.93-1.04)	.58
Multivariate logistic regression with propensity adjustment	1.00 (0.94-1.07)	.89
Stratification based on propensity quintiles	1.00 (0.96-1.05)	.91

Abbreviation: OR, odds ratio.

[a] Each of the alternative analyses was conducted using the full cohort of 60 975 mechanically ventilated medical patients.

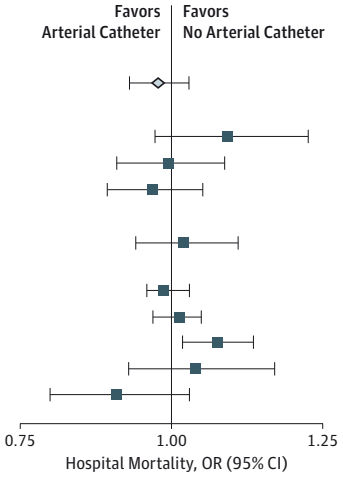
2009 Cochrane review[53] of 5 randomized (and quasirandomized) trials examined the usefulness of continuous-pulse oximetry during anesthesia. Although the American Society of Anesthesiologists mandates the use of continuous pulse oximetry,[54] the Cochrane review[53] found that although oximetry led to a reduction of hypoxemic events in the recovery room, it was not associated with improved morbidity or mortality. Third, data on the use of continuous telemetry monitoring are conflicting. Two cohort studies[55,56] reported that hospitalized patients who have cardiac arrests while undergoing telemetry have higher survival rates than do those who are not monitored. However, a third study[57] demonstrated that only 56% of cardiac arrests were signaled by telemetry and that only 0.02% of patients survived telemetry-signaled arrests. Finally, 2 recent randomized clinical trials investigated the usefulness of intracranial pressure monitors for traumatic brain injury; one found that monitors improved survival[58] and the other found no impact of the device.[59]

For our primary cohort and 8 of the 9 investigated secondary cohorts, we found no association between AC use and outcomes. There are 2 potential interpretations of these results. The first is that there is no mortality benefit associated with AC use for ICU patients. Alternatively, despite attempts to adjust for confounders, residual confounding remains. Were this to be the case, it is plausible that no mortality effect was detected with ACs because patients who receive ACs are more likely to die, which use of ACs ameliorates. The replication of our results across multiple analyses for the primary cohort and multiple secondary cohorts makes this latter explanation less likely. However, concerns regarding residual confounding can never be eliminated in observational analyses.

Monitoring devices come with increased risks and costs. Prior studies[60,61] have found AC use to be associated with more phlebotomy and laboratory testing in the ICU. We did not have access to blood sampling practices for our patients; instead, we used a surrogate marker—PRBC transfusions—to evaluate

Figure. Odds Ratios (95% CIs) for Hospital Mortality Associated With Arterial Catheter Use

Primary Cohorts	No. of Matched Pairs
MV medical patients	13603
MV medical patients by illness severity	
Lowest tertile MPM_0-III	4223
Middle tertile MPM_0-III	4564
Highest tertile MPM_0-III	4783
Secondary cohorts	
MV medical patients in combined medical-surgical ICUs	4336
All patients	47756
All patients in combined medical-surgical ICUs	29014
Patients requiring vasopressors	10840
Patients with septic shock	2358
MV surgical patients	5202



Analyses were done using a propensity-matched strategy. ICU indicates intensive care unit; MPM_0-III, Mortality Probability Admission Model–predicted hospital mortality at ICU admission to third iteration; MV, mechanical ventilation; and OR, odds ratio.

Table 3. Odds Ratios for Additional Procedures Associated With Arterial Catheter Use in Medical Patient Requiring Mechanical Ventilation[a]

Characteristic	No Arterial Catheter		Arterial Catheter		RR (95% CI)[b]	*P* Value for RR[b]
	Received, %	No. of Interventions/d, Median (IQR)	Received, %	No. of Interventions/d, Median (IQR)		
Transfusion						
Packed red blood cells	15.9	0.25 (0.15-0.50)	20.7	0.25 (0.14-0.43)	0.99 (0.82-1.19)	.91
Platelets	3.1	0.50 (0.20-1.43)	3.9	0.59 (0.25-1.50)	0.76 (0.50-1.17)	.21
Paracentesis	1.2	0.14 (0.08-0.25)	1.4	0.12 (0.07-0.22)	1.33 (0.56-3.14)	.52
Lumbar puncture	2.8	0.13 (0.08-0.25)	2.7	0.11 (0.06-0.20)	0.62 (0.35-1.10)	.10
Transesophageal echocardiogram	2.6	0.10 (0.06-0.17)	3.2	0.09 (0.06-0.17)	1.26 (0.67-2.35)	.48

Abbreviations: IQR, interquartile range; RR, rate ratio.

[a] Analyses were done using a propensity-matched strategy; the case-matched cohort was recreated including patients who received mechanical ventilation at some point during intensive care unit (ICU) admission who did not undergo surgery within the 7 days prior to ICU admission and were admitted to the ICU from any location other than the operating room or postanesthesia care unit (primary cohort). Excluded patients included those for whom ICU length of stay data were unavailable and those who received more than 2 U of packed red blood cells on any single day; the number of matched pairs based on these exclusions was 12 796.

[b] Calculated using zero-inflated negative binomial regression (offset by ICU length of stay).

the potential morbidity of AC use as a result of increased phlebotomy. Arterial catheter use did not result in increased PRBC transfusions in our cohort. However, it is possible that increased phlebotomy—and laboratory testing—occurred but was not sufficient to result in excess transfusions. Increased phlebotomy in the ICU has been shown[62] to raise costs without conferring any benefit. In addition, all diagnostic tests have false-positive rates, which frequently result in unnecessary, often invasive, additional testing.[63-67]

The strength of our study stems from the robustness of our results across multiple cohorts and analytic methods. Our study is limited by the fact that receipt of ACs by individual patients was not random, and we cannot exclude the potential for residual confounding, treatment indication bias, or immortal time bias, which would be required to establish causality. Therefore, our findings should be viewed as hypothesis generating similar to the work by Connors et al[48] on pulmonary artery catheters. Because of that initial propensity-matched cohort analysis, numerous randomized clinical trials were performed, none of which supported the belief that pulmonary artery catheters save lives in the ICU.[49-52] Nearly 2 decades later, it may be prudent to embark on a similar set of investigations into the usefulness of ACs.

In addition, our data set did not allow us to assess why patients had ACs placed or how information from ACs was used. Having these data would not have changed our main results, but may have allowed us to better understand possible drivers of use. Our data set included patients admitted from January 1, 2001, to December 31, 2008. Although we know that AC use patterns in ICUs in the United States did not change substantially during that time,[4] it is possible that meaningful change that we could not capture has occurred more recently. Finally, we were unable to identify matching pairs for 43.6% of the patients who had an AC in our primary cohort. The patients with an AC who we could match had statistically significantly different baseline characteristics (eg, fewer vital sign abnormalities on ICU admission, less use of vasopressors and other intravascular catheters, and less multiorgan failure) (eTable 6 in the Supplement) compared with those who had an AC and were unable to be matched. Our final matched

patient cohort, however, was large and representative of ICU patients. Moreover, our matching rates are comparable to those of similar studies.[48,68,69]

Conclusions

Our results suggest that ACs do not improve the ability to care for ICU patients. Monitoring devices are not without cost and potential harms. Therefore, the possibility that a monitoring device may not help patients highlights the need for randomized clinical trials to evaluate this topic. The results from our subgroup analyses may help to identify populations for enrollment, and the magnitude of the associations that we found may assist planners in determining enrollment targets. With careful planning, such randomized clinical trials could address the effect of AC use on mortality as well as on numerous other meaningful patient-centered outcomes.

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