Risk of Arterial Catheter Infections: Do Meta-Analyses Carry Forward Obsolete Data?

To the Editor:

In a recent issue of Critical Care Medicine, with interest we read the meta-analysis by O’Horo et al (1) on arterial catheter-related bloodstream infection (CRBSI). The authors conclude that femoral arterial catheter placement is associated with increased risk of CRBSI.

We disagree for several reasons:

1. Most of these studies are not “true comparative”: They lack randomization and stratification or adjustment for other risk factors for CRBSI, for example, length of placement and severity of patient’s medical condition.

2. Placement of a femoral catheter might be associated with conditions which can themselves be assumed to contribute to worse outcome and infections.
   a. Radial site might be preferred in elective patients with short expected period of unconsciousness and limited need for advanced hemodynamic monitoring.
   b. By contrast, particularly after the introduction of combined transpulmonary thermodilution and pulse contour analysis techniques, femoral access is the preferred site allowing for more elaborate hemodynamic monitoring required for more severely ill patients.

For example, in the study by Lorente et al (Ref. 34 in [1]), most patients with radial catheters underwent elective cardiac surgery, whereas patients with femoral catheters suffered from acute surgical or medical issues. Nevertheless, the number of CRBSI was not elevated in femoral catheters.

3. Ten of the studies classified as “true comparative” did not show an increased risk in femoral catheters. Furthermore, in the 1985 study from Damen et al (Ref. 48 in [1]), we were not able to reconstruct CRBSI rates for radial and femoral site. Therefore, we could not detect data supporting this increased risk for femoral arterial catheters. The same holds true for the study by Norwood et al (Ref. 53 in [1]). The number of femoral versus radial catheters was “uneven” with 8 versus 609 (1.3% vs 98.7%) in 1985 and 1986 studies by Damen et al, respectively (Refs. 24, 48 in [1]).

4. Both studies by Damen et al were performed in the same ICU. The first study analyzed all patients undergoing open heart surgery between January 1, 1983, and January 1, 1985. Since there might be an overlap, we would like to ask the authors if both studies can be used as distinct datasets strongly supporting a questionable conclusion.

5. Despite the merits to analyze studies published within a more than 30-year period, we doubt whether sustainable conclusions for future practice can be derived from nonrandomized studies conducted more than 25 years ago, prior to the introduction of generally accepted hygienic and antiseptic bundles for catheter placement. Figure 2 in the meta-analysis by O’Horo et al (1) demonstrates that the last four studies included and published between 2008 and 2012 did not show an increased risk of CRBSI for femoral catheters with risk ratios between 0.92 and 1.93. By contrast, four studies published between 1985 and 1991 demonstrated risk ratios between 15.5 and 76.1.

To clarify the impact of arterial catheter site for CRBSI, prospective “true comparative” studies at least adjusting for additional risk factors are required.

The work was performed at II. Medical Clinic, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany.

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The authors reply:

Lee et al (1) question the risk of femoral arterial catheter infection in our recent meta-analysis and the contribution of studies by Damen (2), Damen et al (3), and Norwood et al (4). The articles by Damen (2) and Damen et al (3) had overlapping data, resulting in some patients being counted twice. The two studies by Damen (2) and Damen et al (3) were given weights of 0.99% and 1.00%, respectively, in our pooled estimate of infection risk, and thus contributed
very little to the analysis. With regard to Norwood et al (4), the study reported a 0% prevalence of bacteremia associated with positive subcutaneous catheter results, and the overall weighting of this study in our pooled risk estimate was 1.00%, which is also a very small contribution. In keeping with our results, we believe that whenever possible, the radial route should be preferred over a femoral arterial route as recommended in the most recent Healthcare Infection Control Practices Advisory Committee guidelines for prevention of central catheter-associated bloodstream infection (5). We agree that given improved care in insertion and maintenance over the years, the overall risk may be reduced considerably, as was demonstrated for central venous catheters (6) and as Lee et al (1) show in their sensitivity analysis for arterial catheters.

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Does Augmented Creatinine Clearance Accurately Reflect Glomerular Hyperfiltration in Critical Illness?

To the Editor:

In a recent issue of Critical Care Medicine, Udy et al (1) examined the prevalence of augmented renal clearance (ARC), supranormal glomerular filtration in critically ill. They found that 65% of patients with admission serum creatinine less than 120 μmol/L had ARC (creatinine clearance \( [\text{CrCl}] > 130 \text{ mL/min/1.73 m}^2 \)) one or more ICU days up to day 7. Accurate assessment of renal function in critical illness is crucial to appropriate pharmacotherapy; however, in this and previous reports, diagnosis of ARC has relied solely on urinary CrCl. There are two major confounders to interpretation of CrCl: first, systematic overestimation of actual glomerular filtration rate (GFR) by CrCl due to tubular creatinine secretion, and second, large inherent variation in CrCl between serial measurements. I am, therefore, concerned that CrCl could overestimate the true prevalence of ARC and is too imprecise for accurate diagnosis in individual patients.

True CrCl exceeds GFR due to tubular creatinine secretion; however, as traditional colorimetric (Jaffe) assays overestimated serum creatinine (by detection of other chromogens), CrCl was correspondingly underestimated and therefore might reasonably approximate GFR. However, recent international recalculation of creatinine measurements to isotope-dilution mass spectroscopy (IDMS) traceable standards results has, by avoiding overestimation of serum creatinine, allowed more accurate measurement of CrCl, revealing the true extent of overestimation of GFR (2). Udy et al (1) state that tubular creatinine secretion is unlikely to confound estimation of higher GFR by CrCl; however, the supporting reference is from 1972, long before adoption of IDMS standards; furthermore, the citation provided (3) is not to an original publication, but actually to a letter rebutting the use of CrCl as an accurate GFR estimate; those authors having previously shown that, although CrCl overestimates GFR by a greater proportion at lower GFR, it still did so by ~20% at GFR more than 90 mL/min (4). In the era of IDMS, traceability measured CrCl might be expected to exceed true GFR to an even greater extent. In addition, precision of CrCl is also poor, with coefficients of variation (CV) of 10–20% in best conditions, due to compounded imprecision in the two creatinine assays and urine volume required for its calculation (5). Such variation will have a particular significance when examining repeated CrCl measurements for ARC.

To illustrate the potential impact of these factors, I considered a population with mean (± sd) GFR of 101 ± 16 mL/min/1.73 m² (data from healthy kidney donors, mean age 41), in this group only 4% are predicted GFR more than 130 mL/min/1.73 m². However, after simulating 10–20% overestimation of GFR by IDMS-CrCl and accounting for CV of 15% between CrCl measurements, ARC would be diagnosed in 30% of individuals on a single CrCl and in 52% by one or more of four measurements. Thus, healthy individuals, with actual prevalence of “ARC” of only 4%, could show apparent rates of ARC by CrCl not far below those reported in the critically ill.

In conclusion, although transient hyperfiltration may occur in younger patients with a hyperdynamic circulation and recruitable renal reserve, the true prevalence of ARC in the critically ill needs to be confirmed by GFR measurements with greater accuracy and precision than CrCl.

Dr. Prowle consulted for Gambro AB, is employed by Barts Health NHS Trust, and lectured for Gambro AB and Alere. His institution received grant support from Bart and the London Charity.

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