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Impact of definition and procedures used for absent blood culture data on the rate of intravascular catheter infection during parenteral nutrition

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SUMMARY

Background: Diagnosis of intravascular catheter infection may be affected by the definition and procedures applied in the absence of blood culture data.
Aim: To examine the extent to which different definitions of catheter infection and procedures for handling absent blood culture data can affect reported catheter infection rates.
Methods: Catheter infection rates were established in a cohort of hospitalized patients administered parenteral nutrition according to three clinical and four published definitions. Paired and unpaired comparisons were made using available case analyses, sensitivity analyses and intention-to-categorize analyses.
Findings: Complete data were available for each clinical definition ($N = 193$), and there were missing data (4.1–26.9%) for the published definitions. In an available case analysis, the catheter infection rate was 13.0–36.8% for the clinical definitions and 2.1–12.4% for the published definitions. For the published definitions, the rate was 1.6–32.1% in a sensitivity analysis and 11.4–16.9% in an intention-to-categorize analysis, with suggestion of bias towards a higher catheter infection rate in those with missing data, in keeping with the analyses of the clinical definitions. For paired comparisons, the strength of agreement between definitions varied from 'poor' (Cohen's kappa <0.21) to 'very good' (Cohen's kappa ≥ 0.81).
Conclusion: The use of different definitions of catheter infection and procedures applied in the absence of blood culture data produced widely different catheter infection rates, which could compromise measurements or comparisons of service quality or study outcome. As such, there is a need to establish and use a valid, consistent and practical definition.

Introduction

Intravascular catheter infection is a serious complication of intravenous fluid and drug administration, and is costly and

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associated with increased mortality.[1–4] Therefore, there has been considerable investment to reduce the number of catheter infections, and to use the catheter infection rate as a benchmark for the quality of service provision. However, the different criteria used to determine catheter infections could have major effects on the benchmark, and potentially on the ranking order of catheter infection rates by institution. The variability in reported catheter infection rates is surprisingly large, ranging from 0%[5] to >25%[6] in patients administered parenteral nutrition (PN). Furthermore, interventions, such as the introduction of a nutrition team, have been reported to reduce catheter infection rates in such patients by more than an order of magnitude.[1]

Such large variability may be due, at least in part, to the choice of diagnostic criteria used to assess catheter infection, and other methodological differences, such as the extent to which confounding variables and missing data are taken into account. For example, ignoring missing blood cultures, which are required for some definitions of catheter infection, could introduce bias, especially if the missing results did not occur at random. Such factors could be responsible for creating invalid and misleading comparisons between centres and types of intervention.

This study aimed to assess the extent to which the number of catheter infections is affected by different commonly used or recommended definitions, and by different methods for dealing with missing data. A further aim was to make recommendations for clinical practice and research. A patient cohort receiving PN was used to address these aims, as this group is often considered to be at particular risk of catheter infection, due, in part, to potentially enhanced microbial growth in the nutrient-rich PN infusates.

Methods

The study cohort comprised all adult hospital inpatients starting PN in a large UK teaching hospital (Southampton) between December 2009 and July 2010 inclusive. Prior to data collection, the local ethics committee confirmed that no formal approval was required for this study, in which data from medical records were to be obtained retrospectively by one of the authors (PDA).

All new suspected episodes of catheter infection, including those that occurred more than once in the same patient during their hospital stay, were identified from medical records. Suspected catheter infection was defined as temperature ≥38°C and/or documented clinical suspicion of catheter infection for any reason. Sepsis and pyrexia due to other defined sources were excluded. From these suspected episodes, catheter infection was established according to seven commonly used definitions. Two were simple pragmatic clinical markers: removal of the central venous catheter used for PN due to suspected catheter infection; and cessation of PN due to suspected catheter infection. Another was a documented retrospective, multi-disciplinary clinical diagnosis based on clear statements of confirmed catheter infection following investigation of suspected catheter infection. The remaining four definitions were published by various groups from the Hospital in Europe Link for Infection Control through Surveillance (HELICS) (2004),[7] the European Society for Clinical Nutrition and Metabolism (ESPEN) (2009),[8] the Matching Michigan project (2010),[9] and the Centers for Disease Control and Prevention (CDC) (2011,[10] which refers to their 2008 definition[11]). In separate analyses, the 2011[10] and 2002[12] versions of the CDC definition were compared. All methods for diagnosing catheter infection within each published definition were included (Supplementary File I). The catheter infection rate was calculated as catheter infection per PN episode. For the purposes of this paper, the term 'catheter infection' is used to describe 'intravascular catheter infection' where 'infection' is used to indicate the process of infecting or the state of being infected (clinical or subclinical manifestations).

Microbiological assessment of blood cultures and venous catheter tips was undertaken by the hospital pathology department. Each blood culture required 10 mL of blood, and a positive indication from a BacT/ALERT 3D microbial detection system (bioMérieux UK Ltd, Basingstoke, UK) led to a Gram stain that was examined using immersion oil at x100 microscopy and culture on four agar plates (Oxoid Ltd, Basingstoke, UK) for at least 24 h at 37°C: chocolate lysed blood agar and Columbia blood agar, both in a 5% carbon dioxide environment; fastidious horse blood agar in an anaerobic environment; and cysteine-lactose-electrolyte-deficient agar. Growing microbes were identified using relevant Analytical Profile Index kits (bioMérieux UK Ltd), and the British Society for Antimicrobial Chemotherapy guidelines were used to establish sensitivity breakpoints. Each tested venous catheter tip was vortexed in 1 mL of tryptone broth before 100 μL were taken and incubated on a Columbia blood agar plate at 37°C for 48 h. If any growth was detected within 48 h, the guidelines of the British Society for Antimicrobial Chemotherapy were used to establish microbial sensitivity breakpoints.

Two main types of analysis were undertaken to compare catheter infection rates established by two different definitions of catheter infection: unpaired statistical comparisons, in which all the available data were used even if a diagnosis of catheter infection in a particular subject could be established using one definition and not another; and pairwise comparisons, in which the diagnosis had been made by both definitions. With the latter analysis, any subject with missing data in either comparison arm was eliminated (pairwise deletions); for example, due to missing blood cultures that prevented establishment of catheter infection using certain definitions.[7–10] Indeed, in some cases, only one blood culture was required, and in other cases, more than one blood culture or simultaneous central and peripheral blood cultures were required.[7–10,12] A further type of analysis examined the risk of bias associated with the exclusion of subjects due to missing data (i.e. the possibility that excluded subjects differed systematically from included subjects). It also involved both sensitivity and intention-to-categorize analyses. The following two-step procedure was undertaken in order to examine if the missing data (absence of blood cultures) for the published definitions were missing at random. First, the datasets for each of the three clinical definitions with complete datasets were split into two groups; one corresponding to episodes with complete data for a specific published definition, and the other corresponding to episodes with incomplete data for the same published definition. Second, the proportions of catheter infections in these two newly formed groups were compared. In the sensitivity analysis, all episodes associated with inadequate blood cultures were assigned to the catheter infection group (Model A) or the no catheter infection group (Model B). In