All Catheter-Related Candidemia Is Not the Same: Assessment of the Balance between the Risks and Benefits of Removal of Vascular Catheters

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(See the article by Nucci and Anaissie on pages 591–9)

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Ranking as the third to fourth most common cause of nosocomial bloodstream infections, candidemia is a life-threatening infection that occurs in seriously ill patients who usually have ≥1 intravascular catheter [1, 2]. In these patients, candidemia is associated with a high attributable mortality rate—it can be as high as 38% [3]. Under such circumstances, any and all measures that can possibly reduce the rates of morbidity and mortality are often pursued.

Because *Candida albicans* and other *Candida* species adhere avidly to materials used in vascular catheters, removal of vascular catheters is advocated as an adjunctive strategy for treating patients who have catheter-related candidemia [4]. The rationale for such catheter removal is to eliminate a potential nidus of infection that may perpetuate seeding of the bloodstream. Unfortunately, removal of a vascular catheter is not necessarily a benign procedure. Removal of Hickman- or Broviac-type catheters may require another surgical procedure to replace such a catheter after the candidemia is treated. Removal of any type of central venous catheter will often require reinsertion of new catheters, which may be particularly hazardous in a patient who has thrombocytopenia or some other coagulopathy. An additional complication of reinsertion of new catheters is the possibility of pneumothorax. Thus, clinicians who treat patients with catheter-related candidemia are confronted with a dilemma between removal of the catheter and potential increases in morbidity and mortality caused by reinsertion of new vascular catheters. Recent consensus guidelines have recommended removal of vascular catheters in patients with candidemia when it is feasible [5, 6]. Nevertheless, there have been no randomized controlled trials that have prospectively assessed the risk and benefits associated with catheter removal in patients with candidemia.

Nucci and Anaissie are to be commended for their exhaustive analysis of the literature about catheter-related candidemia. They conducted an evidence-based, comprehensive, retrospective analysis to assess treatment outcomes associated with catheter withdrawal. This extensive review of the literature reflects the problems encountered in such an analysis, in which no prospective randomized trials have addressed this question as a primary objective. Despite these limitations, the findings of several studies support removal of vascular catheters when it is feasible in patients with candidemia [7, 8]. The factors weighing in that decision for individual patients are recapitulated by Nucci and Anaissie in a thoughtfully developed algorithm that should prove to be a valuable clinical tool.

An understanding of the pathogenesis and epidemiology of catheter-related candidemia may further facilitate a rational approach for removal of vascular catheters in patients with candidemia. Independent of the vascular catheter, the human alimentary tract is an important source of *C. albicans* in patients with candidemia [9–11]. Molecular epidemiologic studies of isolates of *Candida* species recovered from a given patient reveal strong genetic relatedness between isolates from the alimentary tract and those in the bloodstream [11]. Patients undergoing cytotoxic chemotherapy for treatment of malignancies may sustain mucosal epithelial disruption that allows for translocation of *Candida* species through
the portal bloodstream beyond the liver and into the systemic circulation [10, 12]. Similarly, among patients undergoing gastrointestinal surgery, Candida species may be an important constituent of the microbiologic flora in intraabdominal infections [9].

Candidemia that arises from the alimentary tract and portal venous circulation may enter the systemic circulation to result in secondary infection of the central venous catheter. In this situation, the catheter is the target rather than the source of candidemia, but it may continue to serve as the source of sustained fungemia as organisms proliferate on the catheter surface. Removal of the catheter under these circumstances may improve therapeutic outcome by elimination of an intravascular source of persistent fungemia. A study published elsewhere [13] involving oncology patients found that sustained fungemia was associated with autopsy-proven disseminated candidiasis and increased mortality rates.

Vascular catheters may, however, also serve as a primary source of fungemia [14–16]. This may be especially apparent in the pediatric neonatal intensive care unit, where episodes of candidiasis and candidemia have occurred as a result of contamination in the domes of pressure transducer connections [15]. Further underscoring the propensity for vascular catheters to be contaminated are reports of catheter-related candidemia resulting from contamination of solutions used for total parenteral nutrition and propofol [14, 16]. Well-conducted case-control analyses that used logistic regression analysis have demonstrated that vascular catheters are an important independent risk factor for development of candidemia [17–19]. The relative frequency with which catheter-related candidemia occurs as a result of direct contamination of the intravenous lines is not clear. Nevertheless, this process is likely to be relatively prevalent, because connections in the line may be readily contaminated with Candida species either from patients’ own flora or from the hands of health care providers. Under these circumstances, when the vascular catheter is the primary portal of entry and focus of infection, removal of the catheter seems to be warranted. As a clinical model of Candida infection of vascular catheters, Candida peripheral suppurative thrombophlebitis teaches us that vascular catheter infections may be difficult to eradicate by use of medical therapy alone [20]. This model also indicates that not all types of vascular catheter-related candidemia are the same. Thrombosis and invasion of the vascular wall may further increase the difficulty of eradicating Candida species by medical therapy exclusively. Evidence of thrombosis found by physical examination or by diagnostic imaging (e.g., MRI angiography) of central venous catheters may portend a more refractory case of candidemia.

A positive culture of a blood sample drawn through a vascular catheter does not necessarily signify an infected vascular catheter. Unfortunately, techniques for reliably identifying infected catheters before their removal are lacking. Laboratory systems that could distinguish infected catheters from noninfected catheters may potentially have a major impact on the decision-making process for catheter removal. Differential colony counts from quantitative peripheral-source and through-the-catheter blood cultures that have used lysis centrifugation methods have yielded mixed results [21, 22]. Perhaps an organism as adherent as Candida species will be more predictive of catheter-related bacteremia [21]. More work that focuses specifically on candidemia and differential colony counts is warranted in quantifying central versus peripheral burden. Fungemia with Candida parapsilosis is strongly associated with a direct catheter infection [23] and would indicate catheter removal. As was previously mentioned, the findings of diagnostic imaging studies suggesting suppurative phlebitis warrant catheter removal. Unfortunately, clinicians all too often learn that the vascular catheter is infected by the presence of persistent candidemia. Further adding to the uncertainty of catheter management in patients with candidemia is the management of peripheral vascular lines and arterial catheters.

If candidemia could easily be eradicated and vascular catheters cleared of Candida species by antifungal chemotherapy alone, then decisions regarding removal of catheters would not be as pressing. Certainly, infections due to other pathogens that can be managed effectively with parenteral therapy directly through the lines, such as gram-negative enteric bacilli, do not necessarily require removal of central venous catheters. Unfortunately, sustained fungemia is associated with poor outcome [13], Candida species have a high propensity for adherence to catheter materials, and the resulting infections are often refractory to eradication from indwelling foreign bodies. Yet, if one decides to attempt to eradicate Candida species from the vascular catheter rather than remove the catheter, we suggest that a parenteral agent (e.g., an amphotericin B formulation or fluconazole) be infused through all lumens of the catheter, preferably by splitting the infusion or rotating infusion through each catheter lumen in an multi-lumen vascular catheter. Neither fluconazole nor amphotericin B appears to be particularly effective in reliably eradicating Candida species from vascular catheters. Perhaps the newer echinocandins may provide a more effective intervention in the eradication of Candida infections of the catheter.

Further complicating the analysis of this issue is the self-evident truth that all cases of catheter-related candidemia are not the same. Patients range in their ability to tolerate infections; thus, they will have a corresponding range of benefits and risks associated with the removal of vascular catheters. The principal consequence of failure to promptly remove an infected catheter is that of persistent fungemia and increased risk of seeding of...
target organs. As outlined by Nucci and Anaissie, a thoughtful and systematic approach to considering the ratio of risks of catheter withdrawal to its benefits is warranted. Unfortunately, it is often the more critically ill patient who will fall into the wait-and-see category of Nucci and Anaissie’s algorithm, and it is in just this setting that failure to remove an infected catheter may be the most devastating. Therefore, the clinician is still left with a need to use clinical judgement and intuition. In our opinion, as is also suggested by Nucci and Anaissie, current data indicate that catheter removal should generally be considered early in the management of candidemia.

References


