

# Catheter Infections – What's New?

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## Introduction

Vascular access is an integral part of the supportive care of patients with cancer.<sup>1</sup> The increased utilization of supportive care measures including intravenous antibiotics, hyperalimentation, blood transfusion and frequent blood sampling makes it imperative to procure durable vascular access in patients with cancer. Major complications of central venous catheters (CVC) include infection and thrombosis.<sup>2</sup> Despite their utility in the management of patients with cancer, complications of CVC could be challenging especially in very ill patients. We will address recent information regarding the infectious complications of vascular access devices in patients with cancer.

## Differential Time To Positivity In The Diagnosis Of Catheter Related Bloodstream Infections

Catheter-related bloodstream infections (CRBI) are a frequent complication of CVC. It is estimated that more than 200,000 cases of CRBI occur annually in the United States.<sup>3</sup> The diagnosis of CRBI remains difficult especially in ill patients with cancer that have multiple complications of their cancer or its therapy. Quantitative and semi-quantitative methods of catheter culture have been used to establish the diagnosis of CRBI.<sup>4, 5</sup> Since these methods require the removal of the CVC, they could be impractical at times and might not help to manage the infection.<sup>6</sup> To avoid the removal of CVC several culture techniques have been used to including simultaneous quantitative blood cultures from the CVC and a peripheral vein (PV).<sup>7</sup> Unfortunately, this method is costly and labor intensive and is not widely used in clinical laboratories.

The measurement of differential time to positivity (DTTP) has been reported to be highly diagnostic of CRBI.<sup>8</sup> The differential time to positivity is defined as the difference in the time it takes for a blood culture drawn through a CVC and a culture drawn through a PV to become positive. The DTTP is suggestive of CRBI if the blood culture drawn through the CVC becomes positive 120 minutes earlier than a positive culture drawn simultaneously through a PV. Some investigators have reported that this method is not as useful in diagnosis CRBI in patients with short-term catheters defined as less than 30 days of insertion.<sup>9</sup> Until recently most published studies were small and included a limited number of patients who had simultaneous positive blood cultures from the CVC and PV.

Raad *et al* made a great contribution to the understanding of this blood culture strategy in the management of cancer patients with CVC.<sup>10</sup> These authors analyzed the DTTP in a prospective fashion in a large group of patients at the M.D. Anderson Cancer Center, a tertiary care cancer center. Their study group comprised all patients who had the same organism isolated from blood cultures drawn simultaneously through the CVC and a PV. They used a composite definition according to the Infectious Diseases Society of America guidelines. One-hundred and ninety-one patients with positive simultaneous CVC and PV cultures were included; of those 108 met the criteria of CRBI and 83 had non-catheter-related bacteremias. Catheter-related bloodstream infections were more frequently caused by Staphylococci and less likely to be associated with underlying hematologic malignancies. They concluded that as a diagnostic tool for CRBI, differential time to positivity of 120 minutes or more was sensitive and specific in patients who have short- and long-term catheters. The authors also made the important observation that in the subset of patients who were receiving antibiotic therapy when blood cultures were drawn, the specificity but not the sensitivity of DTTP was lower. This observation will require further study.<sup>11</sup>

## Management Of Central Venous Catheters In Cancer Patients With Candidemia

The impact of CVC removal in the outcome of candidemia has been evaluated in several studies.<sup>12-14</sup> In most studies, catheter removal improved outcome by decreasing mortality or decreasing the duration of fungemia and recurrence of infection. No study has made a clear distinction in terms of the impact of CVC removal on patients with catheter-related candidemia versus those patients with a non-catheter or indeterminate source of fungemia. Recent guidelines for the treatment of candidiasis recommend that initial management of these infections should include removal of all existing CVC's.<sup>15</sup> Nevertheless, there is a study in bone marrow transplant recipients that suggests that CVC removal had the opposite expected effect on the duration of candidemia.<sup>16</sup> Some authors have questioned the conclusion that automatic removal of all vascular catheters to treat all cases of candidemia is necessary.<sup>17</sup> Until recently, no study has analyzed the impact of the catheter removal on the outcome of candidemia in different subpopulations of patients. In addition, no study has made a clear distinction of the impact of CVC removal on patients with catheter-related fungemia versus those with a non-catheter or indeterminate source of fungemia. To determine the need and appropriate timing of catheter removal Raad *et al* reviewed the records of 404 patients with cancer and CVC who developed candidemia during a 6-year period.<sup>18</sup> Of the total of 404 cases of candidemia, 241 (60%) were due to a primary source, 111 (27%) were catheter-related and 52 (13%) were secondary cases of candidemia caused by another source other than the catheter. Multivariate analysis showed that catheter removal  $\leq$  72 hours after the onset of candidemia only improved response to antifungal therapy exclusively in patients with catheter-related fungemia. Clinical characteristics that suggested a non-catheter source of candidemia included disseminated infection, previous chemotherapy (within 1 month), previous corticosteroid therapy and poor response to antifungal therapy. Based on these findings, the authors proposed an algorithm to assist in the decision of explanting CVC in patients with cancer

and candidemia. Without a doubt this study will create a great deal of controversy since many clinicians feel strongly that all catheters should be removed in patients with candidemia regardless of any other clinical findings. Nevertheless, it has to be kept in mind that in many critically ill patients is not practical or possible to change all indwelling catheters. I believe that this is a very important study since it makes an effort to analyze the outcome of different subpopulations of patients with candidemia and tries to apply consistent definitions for CRBI in this setting.

### **Controversy: Do Antimicrobial-Impregnated Central Venous Catheters Prevent Catheter Related Bloodstream Infections?**

Since it is felt that the skin is the primary source of CRBI, efforts have focused on preventing these infections by impregnating CVC's with combinations of antimicrobial agent. However, some authors question the utility of antimicrobial-impregnated CVC's because of concerns about emergence of antimicrobial resistance, cost and questionable efficacy rates. McConnell *et al* reviewed the literature and selected 11 randomized studies that included a control group that received non-impregnated CVC's.<sup>19</sup> These authors evaluated the methodology including the inclusion of key patient characteristics, use of clinically relevant endpoints and molecular relatedness studies. McConnell *et al* could not identify consistent benefits associated with the use of antimicrobial impregnated CVC's in several clinically relevant end points including reductions the rate of CRBSI, duration of CVC retention, therapeutic antibiotic use, duration of hospital or intensive care unit stay and survival. They concluded that more rigorous studies are required to support or refute the hypothesis that antimicrobial-impregnated CVC's reduce the rate or prevent CRBSI.

Crnich and Maki have refuted McConnell's *et al* analysis based on several facts including: that the studies were not powered to address some of the clinical outcomes suggested by McConnell that the studies followed accepted randomization schemes and that McConnell *et al* downplayed the importance of CRBI.<sup>20</sup> Crnich and Maki recognized that many of the studies criticized by McConnell's *et al* have shortcomings but felt that their analysis downplayed a large body of research that demonstrated consistent reduction in CVC-related CRBSI as well as cost-effectiveness. Crnich and Maki stress the point that 2002 Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention recommends that use of antimicrobial impregnated CVC's only in institutions where rates of CRBSI remain  $\geq 3.3$  per 1000 CVC-days despite consistent application of appropriate infection-control practices.<sup>21</sup>

### **References:**

1. Freytes CO: Vascular access problems revisited: the Multinational Association for Supportive Care in Cancer (MASCC) Experience. *Support Care Cancer* 1998; 6:13-19
2. Freytes, CO: Indications and complications of intravenous devices for chemotherapy. *Curr Opin Oncol* 2000; 12:303-307
3. Kluger DM, Maki DG: The relative risk of intravascular device related bloodstream infections in adults (abstract). In: Abstracts of the 39<sup>th</sup> Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, 26-29 September 1999. Abstract no. 514.
4. Maki DG, Weise CE, Sarafin HW: A semiquantitative culture method for identifying intravenous catheter related infections
5. Sheretz, Raad II, Belani A, et al: Three-year experience with sonicated vascular catheter cultures in a clinical microbiology laboratory. *J Clin Microbiol* 1990;28:76-82
6. Widmer AF, Nettleman M, Flint K, et al: The clinical impact of culturing central venous catheters. A prospective study. *Arch Intern Med* 1992; 152:1299-1302.
7. Fan ST, Teoh-Chan CH, Lau KF: Evaluation of central venous catheter sepsis by differential quantitative blood culture. *Eur J Clin Microbiol Infect Dis* 1989; 8:142-144.
8. Blot F, Schmidt E, Nitenberg G et al: Earlier positivity of central venous versus peripheral blood cultures is highly predictive of catheter related sepsis. *J Clin Microbiol* 1998; 36:105-109.
9. Rijners BJ, Verwaest C, Peetermans WF et al: Difference in time to positivity of hub-blood versus nonhub-blood cultures is not useful for the diagnosis of catheter related bloodstream infections in critically ill patients. *Crit Care Med* 2001; 29:1399-1403.
10. Raad I, Hanna HA, Alakech B, et al: Differential time to positivity: A useful method for diagnosing catheter-related bloodstream infections. *Ann Intern Med* 2004; 140:18-25.
11. Farr BM: Catheters, microbes, time and gold standards. *Ann Intern Med* 2004 ; 140 :62-64
12. Rex JH, Bennett JE, Sugar AM et al: Intravascular catheter exchange and duration of candidemia. *Clin Infect Dis* 1995 ; 21 :994-996.
13. Lecciones JA, Lee JW, Navarro EE, et al: Vascular catheter-associated fungemia in patients with cancer: Analysis of 155 episodes. *Clin Infect Dis* 1992 ; 14 :875-883.
14. Eppes SC, Troutman JL, Gutman LT: Outcome of treatment of of candidemia in children whose central catheters were removed or retained. *Pediatr Infect Dis J* 1989; 8:99-104.
15. Rex JH, Walsh TJ, Sobel JD, et al: Practice guidelines for the treatment of candidiasis. *Clin Infect Dis* 2000; 30: 662-678.

16. Goodrich JM, Reed EC, Mori M, et al: Clinical features of and analysis of risk factors for invasive candidal infections after marrow transplantation. *J Infect Dis* 1991; 164:731-740.
17. Nucci M, Annase E: Should vascular catheters be removed from all patients with candidemia? An evidence-based review. *Clin Infect Dis* 2002; 34:591-599.
18. Raad I, Hanna M, Bocktour M: Management of central venous catheters in patients with cancer and candidemia. *Clin Infect Dis* 2004; 38:1119-1127.
19. McConnell SA, Gubbins PO, Annase EJ : Do microbial impregnated central venous catheters prevent catheter related bloodstream infection? *Clin Infect Dis* 2003; 37:65-72.
20. Crnich CJ, Maki DG: Are antimicrobial-impregnated catheters effective ? Don't throw out the baby with the bathwater. *Clin Infect Dis* 2004 ; 38:1287-1292.
21. O'Grady NP, Alexander M, Dellinger EP et al : Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2002; 35:1281-1307.