[News * Analysis * Commentary * Controversy]

September 10, 2013 * Vol. 35 * No. 17

oncology-times.com

ONCOLOGY TIMES

Lippincott Williams & Wilkins Wolters Kluwer Health

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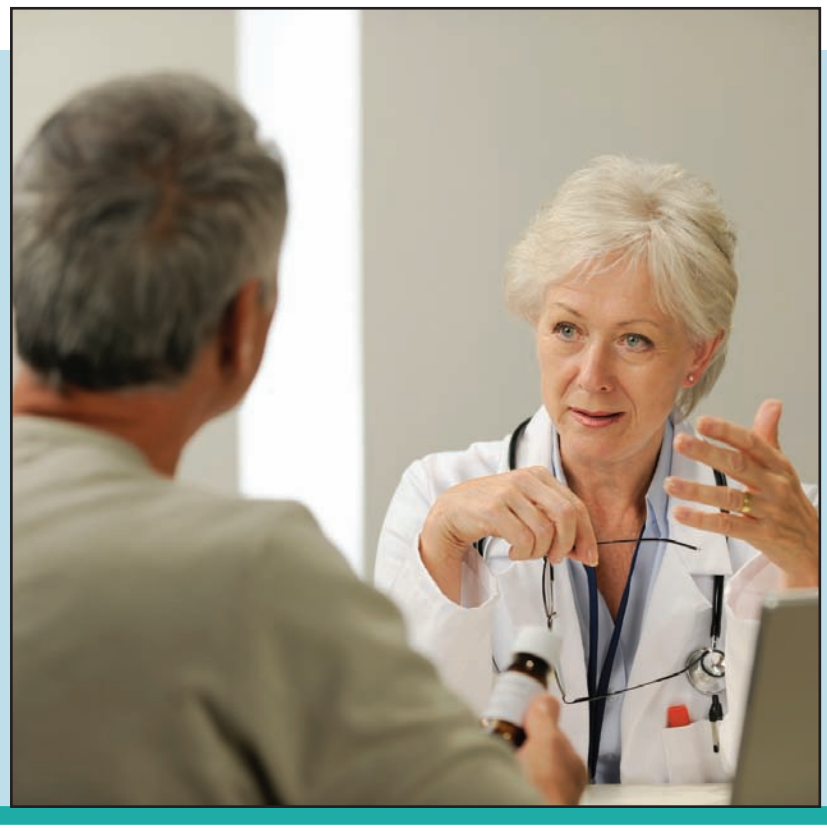


Rethinking When to Say 'Cancer'

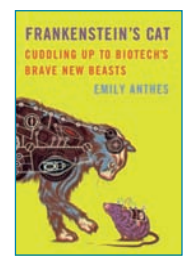
BY ERIC T. ROSENTHAL

Laura Esserman, Ian Thompson, Barry Kramer, Richard Schilsky, Otis Brawley, Robert Mayer, Lynn Schuchter, Mikkael Sekeres, and Ramaswamy Govindan weigh in on the much-discussed *JAMA* article suggesting that the word "cancer" be eliminated from some diagnoses. *Page 16*

Large Study Documents: No Increased Risk for Pregnant Women with Breast Cancer p.8

Post-Academia, Mace Rothenberg Reflects on His Five Years in Industry p.22

In Children with Cancer, Central Line Blood Infections More Common in Ambulatory vs. Hospitalized Patients p.23



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In Children with Cancer, Central Line-Associated Blood Infections Found More Common in Ambulatory than Hospitalized Patients

BY HEATHER LINDSEY

More ambulatory pediatric cancer patients develop central line-associated bloodstream infections (CLABSIs) than their hospitalized counterparts, according to new data. "We've spent a lot of time and resources in an effort to reduce inpatient CLABSIs, but as many as three times the number of outpatients are getting these infections," said the lead investigator, Michael L. Rinke, MD, PhD, Assistant Medical Director of Pediatric Quality at the Children's Hospital at Montefiore in the Bronx, NY, who practiced at Johns Hopkins at the time the research was conducted.

In the study, available online ahead of print in the journal *Pediatric Blood & Cancer* (***doi: 10.1002/pbc.24677***), factors found to increase a child's risk of CLABSI were having a tunneled, externalized catheter; being within 100 days of transplant or less than 30 days from the insertion of the central line; and having a positive blood culture in the central line.

Aditya H. Gaur, MD, Associate Member in the Department of Infectious Diseases at St. Jude Children's Research Hospital, explained that during the last five years, health care providers and administrators have focused on CLABSIs in hospitalized patients. This was for a variety of reasons, including public scrutiny and the decision of the Centers for

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→ROTHENBERG

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But now he has a much larger canvas and that success can be amplified into having an even greater impact on patients. "Everything is put in a larger context, and I have to ask the right questions: Does this move the drug closer to approval? What is its context in terms of other therapies? How relevant is it to us and to the rest of the world? What is the time frame for moving this forward? And how much money should we invest to bring it to market?"

He said other companies have people as smart and dedicated and with as many resources as his group at Pfizer, but what differentiates his team is "paying attention to what's happening elsewhere and having a sense of urgency"—"We want to know how and what others are doing relates to what we are doing. We incorporate all insights into our work and focus on the things we can do.

"In academia you are competing for grants against anonymous entities, but in industry you're competing against known entities, and it's not enough that a compound just be good, it also has to be first and best in its class, and we don't bring drugs forward just because the market is lucrative," he said.

He said that after five years he does believe the trade-offs were well worth it, although he admitted that it took about 18 months before he understood the cycle of the company and could feel fully comfortable knowing what was expected of him within the new culture.

And, now he's ready for the next big change when Pfizer undergoes a restructuring next year that will integrate oncology, vaccines, and consumer health into a single unit with business in "emerging markets" merging with those in the United States, Europe, Japan, and South Korea.

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Medicare & Medicaid Services to not reimburse for certain hospital-acquired infections.

"This paper now indicates that in immune-compromised pediatric patients, the risk of CLABSI does not stop at the hospital walls, and continues in the outpatient setting," he said.

Because of the ambulatory infection risk, "training families how to access central lines and how to take care of the catheter site is very important," said Wilbert Mason, MD, MPH, Attending Physician in the Division of Infectious Disease at Children's Hospital Los Angeles.

Part of the job of oncology services is to help families take care of children who have central lines at home, with the goal of reducing infection, commented Charles Bailey, MD, PhD, an oncologist and Attending Physician at Children's Hospital of Philadelphia and Assistant Professor of Pediatrics at the University of Pennsylvania Perelman School of Medicine. "While the study doesn't give us new ways to make specific changes in educating families, it does remind us that we need to think about this issue in our model for outpatient care."

Study Details

The study, funded by the National Institutes of Health, the Agency for Healthcare Research and Quality, and the Children's Hospital Association, followed 319 ambulatory oncology patients, aged 21 or younger, with central lines at Johns Hopkins Children's Center in Baltimore.

The researchers prospectively identified CLABSIs and retrospectively identified central line days and characteristics associated with infections from January 1, 2009, to October 1, 2010. A total of 55 ambulatory CLABSIs occurred during 84,705 central line days compared with 19 in inpatients during 8,682 central line days, resulting in incidence rates of 0.65 for ambulatory and 2.2 for inpatient CLABSIs per 1,000 central line days.

The absolute number of CLABSIs in the ambulatory setting was 2.9 times higher than in hospitalized patients.

Of the ambulatory patients, 13 percent were admitted to an intensive care unit and 44 percent had their central lines removed due to infection. Thirty-three percent of infections in outpatients were polymicrobial and 56 percent were gram-negative.

WILBERT MASON, MD, MPH

Possibly helpful prophylaxis strategies include the use of antibiotic or ethanol locks, antibiotic-coated catheters, and removing the central line as soon as possible.

MICHAEL L. RINKE, MD, PHD

BRIGITTA MUELLER, MD, CPE, MHCM

Because the CLABSI incidence rate was lower in ambulatory patients than in hospitalized patients due to the number of central line days calculated but the absolute number was higher, the researchers then conducted a secondary analysis adjusting for the type of central line. In that analysis the infection rates were comparable between the two populations (incidence rate ratio [IRR] of 1.6).

This analysis also found that patients with externalized catheters had a significantly greater risk of ambulatory CLABSI than those with totally implantable devices (IRR of 20.6).

In further assessments, 43 incident ambulatory CLABSIs were identified, which were then matched with 86 controls. Bivariable analyses found that ambulatory CLABSI was significantly associated with acute myeloid leukemia (AML) compared with all other diagnoses (odds ratio [OR] of 7).

"This paper shows that in immune-compromised pediatric patients, the risk of CLABSI does not stop at the hospital walls, and continues in the outpatient setting."

Additionally, CLABSI was associated with being less than one month from central line insertion (OR of 2.68), the use of high-intensity chemotherapy (OR of 4.46), having undergone bone marrow transplant within 100 days of infection or clinic visit (OR of 14.5) or a red blood cell or platelet transfusion within one week (OR of 3.1), previous bacteremia in any central line (OR of 6.3), and neutropenia (OR of 5.47).

A multivariable analysis showed that other characteristics were independently associated with ambulatory CLABSIs, including bone marrow transplantation within 100 days (OR of 16), previous bacteremia in any central line (OR of 10) and less than one month from central line insertion (OR of 4.2).

Weighing Risks and Benefits

How physicians should assess the risks and benefits of at-home central lines in pediatric patients is not an easy question to answer, said Brigitta Mueller, MD, CPE, MHCM, Professor in the Department of Pediatrics, Section of Hematology-Oncology at Baylor College of Medicine and Clinic Chief and Director of the Division of Clinical Operations, Quality & Safety at Texas Children's Cancer and Hematology Centers in Houston.

"We put in central lines only if we think the child really needs it," she said. If, for example, the patient has to undergo several cycles of chemotherapy, oncologists may opt for a central line because sticking the veins each time access is needed is not an option. Central lines may also be the best choice if a child needs ongoing parenteral nutrition or antibiotics, she said.

Physicians also weigh the pros and cons about what kind of central line to use because some may carry a higher risk than others, although the risks and benefits may change depending on the child's situation, she added.

Rajaram Nagarajan, MD, MS, Director of Clinical Operations in the Division of Oncology at Cincinnati Children's Hospital Medical Center (CCHMC), said that external catheters are generally used in bone marrow transplant patients requiring high intensity therapy and in children needing frequent line access. A totally implantable device may be appropriate for intermittent therapy and when a patient can tolerate having the line accessed.

One problem that pediatric oncologists face is that the intensity of current chemotherapy regimens means that use of a central venous catheter is often important for safe management of the patient's care overall, Bailey noted. Physicians have few

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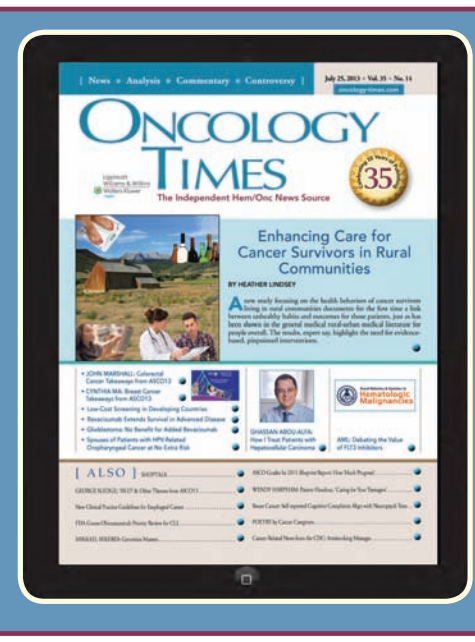

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opportunities to reduce risk by avoiding the central line altogether, he explained.

Another challenge, Mason said, is that this is a particularly high-risk group because of underlying illness and the various types of chemotherapy and radiation treatment patients may be receiving, which diminish immune function. These patients are vulnerable to bacterial and fungal infections that can occur in their central lines, he said.

Prevention Strategies

To help prevent CLABSIs, oncologists should think about using prophylaxis, including antibiotic or ethanol locks, antibiotic coated catheters and removing the central line as soon as possible, Rinke said. "While none of these techniques have been rigorously proven, they are often not harmful and may reduce infections," he said.

It's also important to make sure that the family is capable of providing the best central line care possible. "Families and all ambulatory caregivers need to receive intensive education about how to care for a central line," he said, adding that the best practices used in the hospital can be applied at home, including wearing gloves and scrubbing the hub. If a central line dressing becomes soiled or wet, families need to get their children to a health care provide to get it changed, he said.


RAJARAM NAGARAJAN, MD, MS


JENNIFER M. GOLD, RN

Externally accessible lines also need to be flushed twice daily with heparin, "which requires a lot of education," Mueller said. Patients also benefit from being taught to speak up if they ever see a care provider, whether at home or in-hospital, taking any shortcuts, she added.

> "Training families how to access central lines and how to take care of the catheter site is very important."

Jennifer M. Gold, RN, Clinical Director of the Home Care Agency & Liaison Resource Staff at CCHMC, noted that as part of the infection prevention strategy at the Cincinnati center, home care liaisons educate and train the family in the hospital, prior to discharge, on all aspects of care that will be required at home.

Families learn to use the same protocols and bundles that inpatient nursing staff use, and undergo a self-management assessment at the time of discharge to gauge their competency and comfort level with caring for central lines.

The majority of patients at CCHMC deal with just one home care agency, making consistent practice of infection prevention protocol much easier, Nagararjan noted. Moreover, patients benefit from open collaboration and communication about CLABSIs practices between nurses and physicians and inpatient and outpatient teams.

And, when an ambulatory infection does occur, it is thoroughly investigated by the hematology/oncology clinic, said Kathleen Demmel, RN, MSN, Quality

> "The absolute number of CLABSIs in the ambulatory setting was 2.9 times higher than in hospitalized patients."

Outcomes Manager of the Patient Services Institute at CCHMC. "We see what we could have done better and share this information to try and improve care in the future."

St. Jude offers parents of patients who aren't staying at a local housing facility or who don't have access to a St. Jude affiliate or home care agency extensive one-on-one education from specialized line nurses, said Hana Hakim, MD, Infection Control Officer and Assistant Member of the Department of Infectious Diseases, adding that parents and caregivers are also taught the warning signs of infection and when to seek medical attention.


KATHLEEN DEMMEL, RN, MSN

> "Ambulatory CLABSIs carry appreciable morbidity and have identifiable, associated factors that should be addressed in future ambulatory CLABSI prevention efforts."