A Randomized Controlled Trial Comparing the Rates of Bacterial Colonization of Nontunneled Internal Jugular Vein Catheters and Femoral Vein Catheters.

David Lederer

Lay Abstract

Study Purpose: Many patients admitted to the hospital require one or more venous catheters to be placed. Venous catheters (also known as "lVs" or "intravenous lines") permit the infusion of medications and therapeutic fluids directly into the bloodstream. These catheters (thin plastic tubes) are often placed in a peripheral vein (that is, in the forearm or hand). However, when rapid infusion of fluid or when numerous different fluids and drugs must be administered, a catheter may be placed in a central vein. The central veins include the femoral (thigh) vein and the internal jugular (neck) vein. Central vein catheters (CVCs) are commonly placed in patients requiring care in the Intensive Care Unit (ICU). Although placed at the bedside by interns and residents, CVC placement in more invasive than peripheral "IV" placement and has a number of potential complications associated with it, including a small but definite risk of bloodstream infection. These bloodstream infections have been associated with a 10-20% mortality rate in the literature. Moreover, there is an unfounded "medical myth" that thigh CVCs are associated with a higher rate of bloodstream infection than are neck CVCs. No study has documented this association, and, in fact, a prospective study published in 1991 found no cases of catheter-related bloodstream infection associated with 150 thigh catheters. Contamination of the CVC is a prerequisite for CR-BSI, and its presence is a known risk factor for the development of CR-BSI. We aim to study the rate of bacterial contamination of CVCs in ICU patients randomized to receive either a neck CVC or a thigh CVC.

Study Subjects: We intend to recruit adults admitted to one of four ICUs at CPMC (Medical ICU, Surgical ICU, Cardiothoracic ICU, Neurosurgical ICU) who require central venous catheterization as determined by the ICU physician team. Approximately 660 patients will be enrolled. Patients will be recruited by the ICU physician staff over a 12 month period.

Study Procedures: Subjects who meet entrance criteria will be randomized to receive either neck OR thigh central vein catheterization. These catheters will be placed by the ICU house staff using a standardized protocol (used in the MICU at CPMC and recommended in part by the Centers for Disease Control (CDC)). Each study catheter will be examined daily by a member of the research team. At the first sign of infection, a new catheter will be placed (as indicated clinically), blood will be drawn to grow bacteria (as indicated clinically), and the old catheter will be removed and sent to the microbiology laboratory for routine bacterial culture. Further interventions or diagnostic studies will be performed as the ICU team deems necessary for the medical care of the patient.

Issues: We are randomizing participants who clinically require central vein catheterization to undergo catheterization in one of two accepted anatomic locations (neck or thigh). Since neither procedure is novel and each participant will be receiving the same care they would otherwise receive in the ICU, we do not see a need for informed consent from each patient or his/her proxy or surrogate. Furthermore, a significant fraction of patients are confused, sedated, or comatose upon arrival in the ICU, thereby making informed consent difficult or impossible. Each patient, proxy, or surrogate will receive an information sheet containing information similar to that found in an informed consent form.

IRB Protocol

A. Study Purpose and Rationale

Many patients admitted to the ICU require central venous catheterization (CVC). These catheters are routinely placed in the femoral (thigh) vein and internal jugular (neck) vein by ICU interns and residents at CPMC. A significant complication of CVC is catheter-related bloodstream infection (CR-BSI), which carries a mortality rate of 1020%. Although there is some evidence that CR-BSI is more frequently associated with internal jugular lines than with subclavian vein Oust below the collar bone) lines, no study has compared femoral line CR-BSI incidence to internal jugular line CR-BSI incidence. Nevertheless, there is a "medical myth" that femoral lines result in a higher infection rate than do internal jugular lines.

Encouraging is a prospective single-arm study documenting the incidence of femoral CR-BSI in the ICU (Williams, et. al., Use of Femoral Venous Catheters in Critically III Adults: Prospective Study. *Critical Care Medicine, 19(4): 550-553, 1991.)* No CR-BSI were found in 123 patients with 150 catheters.

In a prospective non-randomized trial, the rates of femoral and internal jugular CRBSI did not differ. However, this study was not powered to detect a difference in incidence rates of CR-BSI.

The presence of bacteria living on the catheter (that is, bacterial "contamination" or C4colonization") occurs frequently in the absence of frank infection. Such contamination is associated with a high risk of infection (indeed, most cases of CR-BSI cannot occur in the absence of catheter contamination). Therefore, catheter contamination may be used as a surrogate marker (risk factor) for CR-BSI.

We intend to conduct a randomized clinical trial comparing the rates of catheter colonization in patients with internal jugular CVCs and femoral CVCs.

B. Study Design

This will be a randorpized, unblinded clinical trial comparing the catheter contamination rate in ICU patients randomized to either internal jugular CVC or femoral CVC for whom CVC is clinically indicated. We intend to enroll 660 patients. The sample size was calculated for a 90% power to detect a difference between a contamination rate of 20% and 10% at a significance level of 0.05.

Results will be analyzed with chi-square analysis or Fisher exact test for proportions. A logistic regression will be performed to identify covariates associated with the presence of colonization. A survival analysis will also be performed to assess the cumulative risk of CR-BSI. Cox proportional hazards model will be used to analyze discrete data sets for factors associated with the cumulative risk of CR-BSI.

C. Study Procedures

The primary study procedure in percutaneous insertion of a short-term non-tunneled CVC at the bedside by a physician member of the ICU staff. This procedure is performed routinely in ICU patients, and no change in procedure protocol will take place within the confines of the study. Briefly, CVCs are placed under sterile conditions using the Seldinger technique to insert a thin polyurethane triple-lumen catheter into a central vein. The Seldinger technique entails venous puncture by a large bore hollow needle through which a wire is threaded into the vein. The catheter is then slipped around (over) the wire and threaded into the vein. The wire is then removed. The procedure takes about ten (10) minutes and is associated with zero to minimal pain after the use of a

local anesthetic. This procedure (including the Seldinger technique) is the standard protocol for CVC placement at CPMC and nationwide. Known complications of CVC include infection, minor and major bleeding, arterial puncture, pneumothorax (air leak in the chest with a collapsed lung), thrombosis (clots in the veins), air emboli (air pulled into the vein causing lung damage), and local discomfort or pain.

Blood draws (up to 40cc or about 3 tablespoons) will be required when infection is suspected. These blood draws will only be performed when clinically indicated, that is, they will only be performed at times when blood draws would be performed outside of the study if the study were not taking place.

Each participant will be involved in the study as long as they possess a study catheter. We anticipate that patients will be involved in the study for 2-10 days. Rarely will a patient be involved in the study for 1-2 months.

The study will conclude after 12 months.

D. Study Drugs

Not applicable

E. Medical Devices

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F. Study Questionnaires

Not applicable

G. Study Subjects

Inclusion criteria are: (1) Hospital location in MICU/SICU/CTICU/NICU or pending transfer to one of the ICUs, (2) clinical decision to place a short-term non-tunneled central venous catheter, and (3) age greater or equal to 18 years.

Exclusion criteria are: (1) blood platelet count <20,000/mm', (2) INR >2.0, (3) PTT >two times the upper limit of normal for PTT, (4) Presence. of a non-study CVC:(neck, groin, peripherally inserted central catheter, long-term central catheter), wwithin'72 hours prior to randomization, (5) recent trauma to neck, groin, or pelvis which contraindicates catheter placement in that area, (6) history of surgery to neck, groin, or pelvis, (7) clinical evidence of skin infection over either catheterization site, (8) Known deep vein thrombosis in both lower extremities, either internal jugular vein, superior or inferior vena cava, (9) Documented catheter-related bloodstream infection in the 72 hours prior to randomization.

Patients meeting all inclusion criteria and no exclusion criteria will be candidates for the study.

Women and minorities will be enrolled in the study in proportion to their ICU admission rate.

H. Recruitment of Subjects

ICU physician staff members (interns, residents, fellows, and attendings) will identify patients in the ICU setting who require CVC placement. No other method of recruitment will be used.

I. Confidentiality of Study Data

A unique coding system (six digit numeral) will be used to identify each patient upon randomization. All study data (including a master list containing name, medical record number, date of birth, and the unique study identifier) will be maintained in Dr. David Chong's locked office in a locked file cabinet. Only Drs. Chong and Lederer will have access to this data.

Study data (without personal identifying data) will be placed in a password-protected computer database accessible only to Drs. Chong and Lederer.

J. Potential Conflict of Interest

None of the study investigators has a proprietary interest in the study device or procedure. Nor do either investigator stand to benefit financially from any result of the investigation.

K. Location of the Study

Patients hospitalized in (or pending transfer to) the Medical ICU, Surgical ICU, Neurosurgical ICU, and Cardiothoracic ICU will be candidates for study enrollment. Patients who are transferred out of one of the above patient care areas will be followed on the wards until the study catheter is removed.

L. Potential Risks

Both study arms are providing standard interventions. There is NO increased risk to the patient who is enrolled in the study. The absence of an increased risk can be attributed to the fact that each study patient would be undergoing CVC if not enrolled in the study.

Known complications of CVC include infection, minor and major bleeding, arterial puncture, thrombosis (clots in the veins), air emboli (air pulled into the vein causing lung damage), and local discomfort or pain. Internal jugular venous catheterization is also associated with a risk of pneumothorax (air leak in the chest with a collapsed lung).

M. Potential Benefit

There is no potential benefit to the study participants.

N. Alternative Therapy

Since patients enrolled in the study require CVC, the alternative would be to not enroll in the study. If not enrolled in the study, patients could undergo subclavian vein catheterization (not performed by medical residents at CPMC), peripheral vein catheterization, or midline catheterization (a slightly longer peripheral vein catheter not routinely used at CPMQ.

O. Compensation to Subjects

Subjects will not receive compensation, monetary or otherwise.

P. Costs to Subjects

No costs relating to the study will be charged to the study subjects. Charges for bacterial cultures will be charged to the patient only when the test is medically indicated. Patients will be responsible for charges incurred by their hospital stay.

P. Minors as Research Subjects

Not Applicable

Q. Radiation or Radioactive Substances

No radiation or radioactive substances will be used in the study. Patients may or may not undergo procedures requiring radiation or radioactive substances as determined by the ICU physicians. Although these procedures will not be a component of the study protocol, the results of such studies may be recorded and included as a data set in the study.

Information Sheet

Columbia Presbyterian Medical Center

Participation in a Research Study

The purpose of this form is to provide you with the information you need to understand the research study in which you are participating.

Study title: A Randomized Controlled Trial Comparing the Rates of Bacterial Colonization of Nontunneled Internal Jugular Vein Catheters and Femoral Vein Catheters.

Study Purpose

You are participating in a research study looking at contamination of intravenous catheters (also known as an "IV") by bacteria and fungus. Studies have shown that catheters that are inserted in the veins (blood vessels) in the neck and thigh have a higher rate of bacterial contamination than those placed in the arm. No study has appropriately compared the rate of contamination of catheters in the neck with the rate of contamination of catheters in the thigh. This study will compare the rates of catheter contamination in those two sites.

You qualify as a participant in this study because you are (or will shortly be) hospitalized in an Intensive Care Unit at Columbia Presbyterian Medical Center (New York Presbyterian Hospital) and your doctor has decided that you require a catheter to be placed in a vein in your neck or your thigh. A total of 660 patients at Columbia Presbyterian Medical Center will be enrolled in this trial.

Study Procedures

An intravenous catheter will be placed in a vein in your neck or in a vein in your thigh. You will be assigned by chance to receive the catheter in your thigh or in your neck. This procedure will be performed by one of the doctors in the intensive care unit, operating room, emergency room, or on the hospital floor. Catheter placement begins with thorough cleansing of the neck or thigh with an iodine-containing solution. Then a sterile sheet is placed over your body, and the doctor will insert a needle into one of the veins in the neck or thigh. A wire will be inserted through the needle into the vein, and a plastic catheter will be threaded over the wire into the vein. The wire in then removed from the vein and the catheter is stitched into place and covered with a clear dressing.

The catheter used and the technique described above are not experimental. Your doctor has already determined that you require a catheter to be placed as described above. Your entry in this study determines only where the catheter will be placed.

Your doctors in the intensive care unit as well as physician members of the research team will monitor you for complications related to the catheter. The doctors in the intensive care unit will determine when you require blood tests and x-rays for your medical care. You enrollment in this study will not result in the performance of any extra or unnecessary tests.

You will be enrolled in this study until the catheter is removed. Usually these catheters remain in place for 1-7 days. Occasionally the catheter will stay in for up to one month or more. The catheter will be removed when medically necessary or when not needed anymore (as decided by you ICU doctor). If you receive another catheter later in you hospital stay, you may or may not be reenrolled in this study.

Study Risks

The risks associated with intravenous catheters are as follows:

(1) Those patients who receive a catheter in the neck are at risk for developing a collapsed lung (pneumothorax). This complication is rare, is routinely screened for after every procedure, and is treatable with a minor bedside procedure. Most patients will not develop a collapsed lung.

(2) Those patients who receive a catheter in the neck are at risk for a rare complication known as "air embolus." This complication occurs when air is pulled into the vein and travels to the lung, blocking blood flow through the lung. Routine precautions are taken to prevent this complication.
(3) Other risks, regardless of the location of the catheter, include infection, bleeding, clots in the veins, placement of the catheter outside of the vein (for example, in an artery or muscle), and local pain and discomfort.

These risks are the same for all catheter placements in the hospital whether or not you are enrolled in this study. You will not be at a higher risk of complications by enrolling in this study.

Study Benefits

You will not benefit personally from this study.

Benefits to society include a better understanding of how catheter location influences the rate of bacterial contamination. The results of this study may help doctors decide which location is preferable.

Costs

No additional cost will be incurred by you for enrollment in this study.

Costs that are incurred by medically necessary care will be billed to you or your insurance company. After your catheter is removed, it will be sent to tne laboratory to look for bacteria. You will only be responsible for the charges related to this test if your doctor would have ordered it outside of the study.

Compensation

You will not receive monetary compensation for your participation in this study.

Confidentiality

Any information obtained during this study and identified with you will remain confidential. All research material which personally identifies you will be kept in a locked office in Milstein Hospital. Only Drs. Chong and Lederer **w'L-'Il** have access to that information.

Questions

If you have any questions, please ask, and we will do our best to answer them. IF you have additional questions in the future, you can reach Dr. Chong at (212) 305-6751.

If you have any questions on your rights as a research subject, you can call the Institutional Review Board at (212) 305-5883 for information.