VENIPUNCTURE AND LYMPHEDEMA

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THE CLINICAL QUESTION
Is it acceptable to perform venipuncture or VAD insertion on the ipsilateral arm after any type of breast cancer surgery? What are the risks of venipuncture on the ipsilateral arm after breast cancer surgery?

DEFINITIONS
Lymphedema – a chronic, debilitating disease; abnormal accumulation of protein-rich interstitial fluid in a generalized or regional location; may occur in any extremity or body part.

Sentinel lymph node (SLN) – the first lymph node(s) where cancer cells are most likely to spread; determined by injection of a radioactive substance or blue dye or both; SLN removal is done with a very small incision through skin over the node. Read more here.

Axillary lymph node dissection (ALND) – a surgical procedure to remove lymph nodes in the axilla or armpit; location and number of nodes removed are determined by diagnostic tests such as positive SLN biopsy. Read more here.
Cellulitis – a bacterial infection in the skin and loose superficial tissue that can easily spread to other tissue; commonly caused by a loss of skin integrity.

BACKGROUND

Lymphedema results from anatomical and physiological changes in the lymphatic system. Primary lymphedema is caused by congenital or hereditary problems; secondary lymphedema is caused by trauma, infection, tumors, chronic venous insufficiency, surgery, and radiation. Breast cancer and its treatment are the primary causes of secondary lymphedema in the United States. ¹

Although lymphedema can be a common occurrence, it is underreported, and few studies provide baseline and follow-up arm measurements. Long-term incidence rates are not known due to lack of studies beyond 5 years. The National Cancer Institute estimates there will be more than 4 million breast cancer survivors in the United States by 2024. ²

Through the years, changes in breast cancer surgery has resulted in fewer patients needing ALND. When ALND and radiation are combined, reported rates are between 25-40%. ² Other studies report rates between 6% to 65%. About 75% of cases are reported to occur within the first 2 years after surgery and up to 90% by the third year. The risk decreases over subsequent years but never goes away completely. ³ Breast cancer patients are now living longer, consequently driving the need for greater attention to evidence-based strategies to diagnose, prevent, and treat lymphedema.

The International Society of Lymphology issued a staging scale for lymphedema in 2016. Stage 0 is subclinical without edema in an “at risk”
patient. Stage 1 is usually pitting edema that responds to treatment such as arm elevation. Stage 2 is edema that is only partially reduced by treatment and Stage 3 is elephantiasis with skin lesions and recurring infections. Other symptoms include pain, tenderness, soreness, and aching; feelings of heaviness, tightness, and stiffness; numbness; and fatigue. Quality of life is seriously diminished when trying to manage lymphedema, plus it dramatically increases the cost of care.

LYMPH SYSTEM

Lymphatic vessels begin in the peripheral tissues and run parallel to the circulatory system. Lymph nodes are small, oval structures containing multiple small channels. These vessels collect excess interstitial fluid and return it to the bloodstream. The two systems converge in the base of the neck where the lymph vessels join the subclavian vein near its junction with the internal jugular vein. Both sides of the neck have a thoracic duct, although the larger one is on the left side. Lymphatic vessels are very permeable to large molecules, accommodating about 8 liters of a protein-rich clear fluid daily.

Lymphedema occurs when the interstitial water and protein are not absorbed back into the venous capillary system. There are two reasons - an increase in the volume of lymph fluid and a decrease in the transport capacity of the lymph system. When the volume of lymph fluid exceeds the ability of the system to transport it, fluid accumulates in the tissue producing interstitial edema.
Anatomical and physiological changes create mechanical insufficiency and is the most common cause of cancer-related lymphedema.\(^1\)

The lymphatic system has been permanently damaged; therefore, lymphedema is not a curable disease. In the subclinical state, the extremity may not appear edematous, however fluid may be collecting in the tissue. Long term outcomes include lymphostatic fibrosis seen as inflammatory skin changes and impediment to the circulation of macrophages and lymphocytes that increase risk of cellulitis and other tissue infection.\(^1\)

Lymphedema can occur in the breast and ipsilateral upper extremity due to surgery and radiation. The lowest rates are seen with lumpectomy alone; SLN biopsy and radiation produces slightly more risk; and ALND plus radiation produces the highest risk. Additional risk factors include increased body mass index and tumor location in the upper outer breast quadrant. Women under the age of 60 years and those with larger bra cup sizes have higher likelihood of lymphedema.\(^1\)

There is a lack of agreement on the pathophysiology of breast cancer related lymphedema. Many cite the fact that lymphedema may occur many years after the breast cancer treatment, indicating that anatomical changes alone would not be the only cause. Because of this knowledge gap, effective treatment strategies are also limited. Risk factors for lymphedema are known but there is a lack of quality studies on prevention methods.\(^3,6\)

**EVIDENCE**

A literature search on Google Scholar from 2010 to 2018 used these search terms alone and combined:

- lymphedema
• breast cancer related lymphedema
• venipuncture

The search produced four systematic literature reviews focusing on risk reduction strategies for lymphedema. All four reviews agreed that there are limitations in the available studies including small patient populations, reliance on the patient’s ability to recall skin puncture events, retrospective data collection, and single facility reports. While recommendations for risk-reduction methods use clinical reasoning, there is a significant lack of scientific support. 3,6-8

Two types of patients must be considered – those that present with a medical diagnosis of lymphedema and those that are at-risk for lymphedema due to their previous surgical and radiation treatments for breast cancer.

Avoidance of all needle punctures in both types of patients is one of the most prevalent methods discussed, and dates back to 1921. This recommendation was based on a theory that infection was the cause of swelling in the arm following breast cancer surgery. 6 It has now been almost 100 years since that first hypothesis was presented. We have greater knowledge of the lymphatic system and yet there are still significant limitations in our knowledge about lymphedema.

These literature reviews easily point to conflicts among studies. They highlight numerous studies that have shown no relationship between skin puncture and lymphedema while pointing to a prospective study published in 2005 that reported a 2.44-fold risk of lymphedema for women experiencing skin puncture while in the hospital. The negative aspect of this study was reliance on the patient’s ability to recall having skin punctures and no association between the time of puncture and lymphedema development. 8
Studies have failed to establish a cause and effect relationship between skin puncture and lymphedema, yet focus on the risk associated with infection, mainly cellulitis. The act of puncturing skin and the vein in a controlled manner may or may not have a high level of risk for causing lymphedema, but there is one troubling aspect of these studies. No effort has been made to separate the types of venipunctures being done – a simple venipuncture to obtain a blood sample or a venipuncture to insert a peripheral IV catheter into the vein for subsequent infusions. These are very different procedures and have different risk for infection.

All skin infections, especially cellulitis receives a large amount of attention in the lymphedema literature. Several studies have made an association between skin infection and lymphedema, yet none have reported a statistically significant relationship. It is thought that cellulitis and lymphedema may have a cyclic relationship with one causing the other although this has not been confirmed. It is a wise recommendation to closely monitor skin on the at-risk extremity and work to prevent injuries that can lead to skin infections. 8

The connection between lymphedema and skin infections/cellulitis raises serious questions about venipuncture for insertion of any type of peripheral vascular access device. All venipunctures require breaking the skin and skin can never be rendered sterile regardless of the type and application techniques of skin antisepsis.

Knowledge of all types of infections from peripheral catheters is also lacking. A literature review on infections in short peripheral catheters found reports of 4 types of infections

- local cellulitis or soft tissue infection
- phlebitis or thrombophlebitis with 3 known causes – mechanical, chemical, and bacterial, yet there has been very little effort to differentiate between these causes
- suppurative thrombophlebitis
- bloodstream infection 9
The focus on bloodstream infections associated with all types of VADs has received virtually all the attention, although there is some data on location infections. An Italian study reporting a rate of 2.3% of local infections and several case studies have been reported. Colonization of peripheral catheters at removal is estimated to be between 5% and 25%, yet these high rates of colonization are not associated with infections. 9

Thrombophlebitis is reported as high as 80%9; infectious phlebitis is reported in up to 5% of patients with suppurative thrombophlebitis in as many as 2% of patients with short peripheral catheters. Helm also suggests that the majority of catheter related infection data focuses on criteria for bloodstream infection. Bacterial contamination of local peripheral catheter sites may have lower rates but be equally as important clinically. Localized catheter complications of phlebitis, thrombosis, and infiltration begins with the inflammatory process which can progress to become an infectious process. 10

Patients with lymphedema have an increased risk from an inflammatory process due to the change in circulating macrophages and lymphocytes. Inflammatory and infectious processes could trigger lymphedema in patients that are at risk due to their treatment history.

The literature reviews also call attention to the problem of excessive reliance on the contralateral upper extremity for all venipunctures. Use of only one arm for all venipunctures lead to extreme difficulty and reduced success rates. Inserting peripheral catheters into a vein of the foot is not an acceptable alternative due to higher risk factors in those locations. An alternative may be insertion of a central venous access device however that carries much higher risk of infection and thrombosis. Finally, patients with bilateral axillary surgery would prohibit use of both upper extremities for venipuncture. The authors of these papers state that complete avoidance of the at-risk extremity is no longer appropriate. 3 7,8
**PRACTICE RECOMMENDATIONS**

For many years, patients have been told to avoid all needle sticks, venipunctures, and blood pressure cuffs on the ipsilateral arm. Current published guidelines call for avoidance of using the ipsilateral arm for venipuncture. However one analysis of clinical practice guidelines found some low level evidence that the complete avoidance of venipuncture and IV access in an ALND extremity can be relaxed.\textsuperscript{11}

- **Infusion Therapy Standards of Practice, 2016, Infusion Nurses Society\textsuperscript{12}** recommends
  - Avoidance of veins on the ipsilateral side of breast surgery with axillary node dissection and those with lymphedema.

- **Access Device Standards of Practice, Oncology Nursing Society, 2017\textsuperscript{13}** recommends
  - Sites to avoid includes extremities or sites with impaired circulation or injury, lymphedema or axillary lymph node dissection.

- [National Lymphedema Network (NLN)]\textsuperscript{14} writes position paper for patients and professionals recommending:
  - use of a non-affected limb, if possible
  - informing phlebotomist if ipsilateral arm cannot be avoided
  - asking for an experienced phlebotomist
  - not allowing multiple or traumatic punctures

While the NLN recommendations takes a pragmatic approach by providing guidance on use of the affect arm, the use of “phlebotomist” implies venipuncture for blood sampling only and not insertion of a peripheral catheter.
Considerations for clinical decisions about use of an extremity with or at risk for lymphedema include:

1. The need for collaboration between surgeons, oncologists, and infusion nurse/vascular access specialists.
2. Creating a culture of vein preservation in each facility for all patients.
3. A well written policy addressing the criteria for making patient-specific clinical decisions for possible venipuncture of the affected extremity including
   a. Knowledge of the type and extent of surgical resection of the axillary area
   b. Knowledge of use of post-operative radiation.
   c. Patient weight as obesity is associated with greater risk for lymphedema
   d. Purpose of the venipuncture – blood sampling or catheter insertion
   e. Assessment of alternative sites and types of vascular access and the risk presented by each for each patient (e.g., catheter-associated vein thrombosis in a cancer patient)
4. Venipuncture of affected arms ONLY by infusion nurse/vascular access specialist
5. Use of vascular visualization technology (e.g. near infrared light or ultrasound) to locate peripheral veins
6. Strict prohibition of multiple venipuncture attempts and subcutaneous probing for the vein.
7. Use of sterile technique for insertion of all peripheral catheters into the at-risk arm if this type of catheter presents the lowest risk to the patient.

Please obtain and review the following publications to gain a thorough understanding of these issues and as guidance for crafting a policy and procedure for your facility.
REFERENCES


