

Lymphedema Precautions: Time to Abandon Old Practices?

Soojin Ahn and Elisa R. Port, *Mount Sinai Medical Center, New York, NY*

See accompanying article on page 691

The Oncology Grand Rounds series is designed to place original reports published in the Journal into clinical context. A case presentation is followed by a description of diagnostic and management challenges, a review of the relevant literature, and a summary of the authors' suggested management approaches. The goal of this series is to help readers better understand how to apply the results of key studies, including those published in Journal of Clinical Oncology, to patients seen in their own clinical practice.

A 46-year-old premenopausal woman with a body mass index of 21 was found on screening mammography to have a new, approximately 1-cm spiculated mass with associated calcifications in the upper outer quadrant of the left breast. Stereotactic core biopsy showed a focus of invasive duct carcinoma, strongly positive for estrogen and progesterone receptors and negative for human epidermal growth factor receptor 2, with associated ductal carcinoma in situ. Clinical examination revealed no palpable mass or axillary lymphadenopathy. She underwent a left lumpectomy with seed localization and sentinel lymph node biopsy. Final pathology revealed an 8-mm well-differentiated invasive carcinoma without lymphovascular invasion and intermediate grade ductal carcinoma in situ. The margins were clear, and three sentinel lymph nodes were negative for metastasis. The 21-gene recurrence score was 10, suggesting a 7% risk of 10-year distant recurrence with adjuvant endocrine treatment. After the completion of adjuvant radiotherapy (42.50 Gy in 16 fractions to the breast), the patient has returned for a follow-up visit. She is a professional violinist and would like to know what she can do to prevent lymphedema on her upcoming flight to Vienna.

CHALLENGES IN DIAGNOSIS AND MANAGEMENT

Upper extremity lymphedema is a potentially debilitating condition after axillary treatments—surgery or radiotherapy—in patients with breast cancer. Fortunately, lymphedema rarely interferes with daily activities for breast cancer survivors. However, the fear of lymphedema can impede physical activity and lead to avoidance of activities,¹ and the possibility of developing lymphedema can be a source of great anxiety for some patients. Over the years, a variety of anecdotal precautionary measures, such as avoiding blood pressure cuffs, blood draws, and injections in the ipsilateral arm, have been adopted to prevent lymphedema. However, few data support the effectiveness of these measures.

Studies have repeatedly shown that patients who undergo full axillary dissection and regional adjuvant radiation therapy are at higher risk.²⁻⁴ Obesity and infection also increase the chances of developing lymphedema. However, not all such patients develop lymphedema, and it is not known if there are any distinguishable causative factors in those who do. For women who do develop lymphedema, the timing of onset of symptoms is highly variable and unpredictable. Although most commonly seen within 2 to 3 years of axillary surgery, lymphedema can develop at any time, even decades after completion of breast cancer treatment.^{4,5}

Once the diagnosis has been made clinically, there are some ways to control the symptoms, such as physical therapy and use of compressive garments. Although these measures may ameliorate symptoms and improve the quality of life, they are palliative in nature, and there are no proven effective methods to reverse the process.⁶ Therefore, once it develops, lymphedema becomes a chronic condition without cure.

SUMMARY OF THE RELEVANT LITERATURE

Incidence of Lymphedema

A recent meta-analysis revealed that up to 21.4% of women will develop lymphedema after breast cancer surgery, consistent with previous estimates.³ The risk seems to be greatest in the first 2 years after the diagnosis or surgery and likely extends beyond that time period.^{3,4} It should be noted that the reported overall incidence varies greatly, ranging from 2% to greater than 50%,^{2-4,7} likely due to the vast differences in methods and definitions for diagnosis, some of which are indirect measures. Most commonly used methods include objective approaches such as measurement of arm circumferences, water volume displacement, and bioimpedance spectroscopy, but some use highly subjective methods such as self-reports.^{3,8} As expected, each method has different

sensitivity for detecting lymphedema, with arm circumference measurements generally considered the most reliable.⁸ Even with this method for detecting lymphedema, however, there are limitations, such as lack of standardized location for arm measurements or the time intervals at which measurements are taken. In addition, not all studies take into account other reasons for changes in arm circumference, such as change in overall body composition as a result of change in diet and activity levels, further reducing the reliability of this method.⁸

Evolution of Axillary Staging in Patients With Breast Cancer

The wide adoption of sentinel lymph node biopsy (SLNB) for staging in patients with breast cancer with clinically negative axillae significantly reduced the rate of developing lymphedema by sparing a majority of patients with negative nodes axillary lymph node dissection (ALND). With fewer lymph nodes excised, there is less disruption of lymphatic channels, the presumed cause of lymphedema. The reported incidence of lymphedema in patients who undergo SLNB is approximately 5%, as compared with 20% to 30% in those who undergo ALND^{3,4} (Table 1). Widening indications for SLNB have increased the number of women (and men) with breast cancer who can be spared completion axillary dissection and are thus at lower risk of developing lymphedema. Recent findings from important surgical trials have extended the option of omission of completion ALND in some women with positive sentinel lymph nodes²⁷ and offering SLNB after neoadjuvant chemotherapy for patients with initially node-positive cancer.²⁸ Thus, the expanding role of SLNB alone is likely to lower the incidence of lymphedema.

Lymphedema Prevention

Avoidance of needle stick and other trauma. Patients are often advised to avoid nonaccidental skin punctures, such as intravenous sticks and blood draws, in the ipsilateral arm after axillary surgery to prevent any source of entry point for infectious organisms and potential infection and inflammation. Many health care facilities have a policy against blood draws and injections in the ipsilateral arm, and precautionary wrist bands are placed on patients after any axillary surgery for those who are admitted. In some instances, patients and health care providers go to great lengths to exercise these precautions, which can create undue anxiety. The role of puncture wounds in the development of lymphedema, however, is largely a conjecture, and several studies, including the prospective study accompanying this article, indicate that skin punctures do not cause lymphedema.²⁹⁻³¹

Compression prophylaxis for air travel. Air travel is frequently cited as a possible cause of lymphedema. The rapid changes and sustained low cabin pressure during a flight have been cited as culprits. As a result, patients are sometimes advised to wear compression sleeves for prolonged air travel as a preventative measure against lymphedema. However, there is no evidence base supporting the theory that air travel increases risk of lymphedema. When the presence of lymphedema was assessed in women who had reported being on flights after axillary surgery, there was no difference in the incidence from that of women who had not flown.^{30,32} Graham³³ assessed the use of prophylactic garments during flights and found that patients who took precautions when flying were more likely to have clinic-recorded lymphedema than those who did not take precautions, therefore recommending abandonment of this practice.

Table 1. Summary of Lymphedema Incidence/Prevalence and Time Path After SLNB in Select Studies With Objective Measures

First Author	N	Lymphedema Assessment Method	Incidence of Lymphedema in SLNB (%)	Time Points and Follow-Up
Armer ⁹	9	Circumference measurement	22.2	4-14 months; median, 8.5 months
Ashikaga ¹⁰	2,008	Water displacement	16.7	Baseline, 6, 12, 18, 24, 30, and 36 months
Celebioglu ¹¹	30	Water displacement	0	Baseline, 1, 2, and 3 years
Goldberg ^{12,13}	600	Circumference measurement	5	2.7-8 years; median, 5 years
Golshan ¹⁴	77	Circumference measurement	2.6	Minimum 1 year
Haid ¹⁵	57	Circumference measurement	3.5	14-60 months; mean, 25 months
Langer ¹⁶	449	Circumference measurement	3.5	11-62 months; mean, 31 months
Leidenius ¹⁷	92	Circumference measurement	1	3 years
Lucci ¹⁸	446	Circumference measurement	5.5-7.7	Subjective: 6, 12, > 12 months Objective: 30 days; 6, 12 months
Lumachi ¹⁹	54	Circumference measurement	3.7	18-28 months; mean, 22 months
McLaughlin ^{4,20}	600	Circumference measurement	5	2.7-8 years; median, 5 years
McLaughlin ²¹	67	Circumference measurement Interview	2-3 5-6 6-11	6, 12 months
Ozcinar ²	80	Circumference measurement	1.9-8	Midterm: 9-12 months Late term: > 12-64 months
Paim ²²	48	Circumference measurement	4.2	6-60 months; mean, 23 months
Schulze ²³	31	Circumference measurement Water displacement	15.8 10.5	Mean, 49 months
Velloso ²⁴	45	Circumference measurement	4.4	10-42 months; mean, 21.3 months
Wilke ²⁵	4,069	Circumference measurement	0-7	30 days, 6 months

NOTE. Data adapted.²⁶

Abbreviation: SLNB, sentinel lymph node biopsy.

The most current National Lymphedema Network (NLN) position statement on risk reduction states “Consider the pros and cons of wearing compression garments during air travel before making a decision...The NLN cannot specifically recommend or not recommend compression garments for prophylaxis in at-risk people who have not yet developed lymphedema.”³⁴

Physiotherapy and manual lymphatic drainage. Physiotherapy and manual lymphatic drainage are commonly used to prevent lymphedema, but there are conflicting reports on whether they are effective. A small randomized controlled study evaluating effects of early physiotherapy intervention using various exercise regimens including resistance training, stretching exercises, strength exercises, and aerobics done in a progressive manner for 8 weeks did not show any difference in changes in arm circumference or volume but reported significant increase in quality of life.⁶ Two other randomized controlled studies reported more promising results with significantly lower rates of lymphedema with physiotherapy and lymphatic drainage methods^{35,36}; however, the follow-up period was relatively short, ranging from 12 to 24 months.

Surgical approaches. Surgical approaches to reduce the risk of developing lymphedema have been investigated. One technique, axillary reverse mapping, aims to identify and protect the lymphatic drainage specific to the arm during axillary surgery. Arm lymphatics are mapped by injection of blue dye directly into the arm, whereas axillary lymph nodes draining the breast are identified by subareolar injection of technetium sulfur colloid. The authors reported low crossover rates of arm and breast lymphatics and lymph nodes, thereby allowing preservation of the arm lymphatics in some cases, and authors of these studies reported reduced rates of lymphedema.^{37,38} However, blue (arm) lymphatics were identified in only 33.7% of patients, and there were some blue and hot nodes with malignancy on final pathology, limiting the potential value of axillary reverse mapping in reducing the risk of lymphedema to a small proportion of cases. The oncologic safety of this technique in patients with large disease burden in the axilla has also been questioned.³⁹

The lymphatic microsurgical preventing healing approach^{40,41} involves intraoperative identification of the arm lymphatics by injecting blue dye into the arm and clipping them near the insertion to the nodal capsule. After standard ALND is performed, the lymphatic vessels are anastomosed to collateral branches of the axillary vein with intact valves by plastic surgeons. In the small number of successfully treated patients after ALND, the lymphedema rate was significantly lower at 12.4% when compared with unsuccessfully treated patients, 50% of whom developed lymphedema. However, the procedure was successful in only a small number of patients, and the mean follow-up was only 6 months. The lymphatic microsurgical preventing healing approach is performed by highly trained plastic surgeons specialized in microvascular surgery, which may limit its availability.

SUGGESTED APPROACHES TO MANAGEMENT

Lymphedema prevention is an understandable goal for nearly all women with breast cancer. The current study by Ferguson et al,³⁰ a rigorous, prospective trial examining the putative risk factors for

Table 2. Recommendations for Patients After Axillary Surgery

Evidence-Based Recommendations
To avoid weight gain
Regular exercise
Healthy diet
To avoid infection
Timely first aid
Immediate identification and treatment of infection
Skin care
Continue
Air travel
Blood pressure measurements
Exercise

lymphedema, provides further strong evidence for abandoning recommendations regarding preventive behaviors. There are simply no data to suggest that blood pressure cuffs, venipuncture, compression sleeves, routine air travel, or more elaborate physiotherapy or lymphatic surgery affect the chances of developing lymphedema. Although these measures can be exercised at the discretion of the patient, they should be implemented with the knowledge that most current evidence points toward no benefit of avoiding these behaviors and that the exact pathophysiology of lymphedema after axillary surgery is unknown.

Only weight gain and infections have been shown to be true risk factors for developing lymphedema.^{4,30,31} Therefore, patients should be advised to maintain an active lifestyle and avoid weight gain, with emphasis on regular exercise and healthy diet (Table 2). Registered dietitians are great resources and can help guide patients and assist with maintenance or reduction in weight, particularly during the postoperative and survivorship period. As for other preventative behaviors, patients should be informed that there are not enough data to justify recommending strict adherence to avoiding skin punctures, blood pressure measurements, or use of compressive garments for air travel.

With regard to our patient, she was counseled that she is at low risk for developing lymphedema on the basis of having had an SLNB, as opposed to ALND, and because she maintains a healthy body weight. She was further counseled that a compressive garment was not advised for her planned travel, given the lack of data showing an increase in risk of lymphedema related to flying or a reduction in that risk related to wearing a compression sleeve. At 4 years from surgery, she is free of any symptoms of lymphedema and continues to travel widely.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

AUTHOR CONTRIBUTIONS

Manuscript writing: All authors

Final approval of manuscript: All authors

REFERENCES

1. O'Toole JA, Ferguson CM, Swaroop MN, et al: The impact of breast cancer-related lymphedema on the ability to perform upper extremity activities of daily living. *Breast Cancer Res Treat* 150:381-388, 2015
2. Ozcinar B, Guler SA, Kocaman N, et al: Breast cancer related lymphedema in patients with different loco-regional treatments. *Breast* 21:361-365, 2012
3. DiSipio T, Rye S, Newman B, et al: Incidence of unilateral arm lymphoedema after breast cancer: A systematic review and meta-analysis. *Lancet Oncol* 14:500-515, 2013
4. McLaughlin SA, Wright MJ, Morris KT, et al: Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: Objective measurements. *J Clin Oncol* 26:5213-5219, 2008
5. Petrek JA, Senie RT, Peters M, et al: Lymphedema in a cohort of breast carcinoma survivors 20 years after diagnosis. *Cancer* 92:1368-1377, 2001
6. McKenzie DC, Kalda AL: Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: A pilot study. *J Clin Oncol* 21:463-466, 2003
7. Hayes SC, Johansson K, Stout NL, et al: Upper-body morbidity after breast cancer: Incidence and evidence for evaluation, prevention, and management within a prospective surveillance model of care. *Cancer* 118:2237-2249, 2012(suppl 8)
8. Hayes S, Janda M, Cornish B, et al: Lymphedema secondary to breast cancer: How choice of measure influences diagnosis, prevalence, and identifiable risk factors. *Lymphology* 41:18-28, 2008
9. Armer J, Fu MR, Wainstock JM, et al: Lymphedema following breast cancer treatment, including sentinel lymph node biopsy. *Lymphology* 37:73-91, 2004
10. Ashikaga T, Krag DN, Land SR, et al: National Surgical Adjuvant Breast, Bowel Project: Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection versus axillary dissection. *J Surg Oncol* 102:111-118, 2010
11. Celebioglu F, Perbeck L, Frisell J, et al: Lymph drainage studied by lymphoscintigraphy in the arms after sentinel node biopsy compared with axillary lymph node dissection following conservative breast cancer surgery. *Acta Radiol* 48:488-495, 2007
12. Goldberg JL, Wiechmann LI, Riedel ER, et al: Morbidity of sentinel node biopsy in breast cancer: The relationship between the number of excised lymph nodes and lymphedema. *Ann Surg Oncol* 17:3278-3286, 2010
13. Goldberg JL, Riedel ER, Morrow M, et al: Morbidity of sentinel node biopsy: Relationship between number of excised lymph nodes and patient perceptions of lymphedema. *Ann Surg Oncol* 18:2866-2872, 2011
14. Golshan M, Martin WJ, Dowlatshahi K: Sentinel lymph node biopsy lowers the rate of lymphedema when compared with standard axillary lymph node dissection. *Am Surg* 69:209-11, 2003; discussion 212
15. Haid A, Kuehn T, Konstantiniuk P, et al: Shoulder-arm morbidity following axillary dissection and sentinel node only biopsy for breast cancer. *Eur J Surg Oncol* 28:705-710, 2002
16. Langer I, Guller U, Berclaz G, et al: Morbidity of sentinel lymph node biopsy (SLN) alone versus SLN and completion axillary lymph node dissection after breast cancer surgery: A prospective Swiss multicenter study on 659 patients. *Ann Surg* 245:452-461, 2007
17. Leidenius M, Leivonen M, Vironen J, et al: The consequences of long-time arm morbidity in node-negative breast cancer patients with sentinel node biopsy or axillary clearance. *J Surg Oncol* 92:23-31, 2005
18. Lucci A, McCall LM, Beitsch PD, et al: American College of Surgeons Oncology Group: Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol* 25:3657-3663, 2007
19. Lumachi F, Basso SM, Bonamini M, et al: Incidence of arm lymphoedema following sentinel node biopsy, axillary sampling and axillary dissection in patients with breast cancer. *In Vivo* 23:1017-1020, 2009
20. McLaughlin SA, Wright MJ, Morris KT, et al: Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: Patient perceptions and precautionary behaviors. *J Clin Oncol* 26:5220-5226, 2008
21. McLaughlin SA, Bagaria S, Gibson T, et al: Trends in risk reduction practices for the prevention of lymphedema in the first 12 months after breast cancer surgery. *J Am Coll Surg* 216:380-389, 2013; quiz 511-513
22. Paim CR, de Paula Lima ED, Fu MR, et al: Post lymphadenectomy complications and quality of life among breast cancer patients in Brazil. *Cancer Nurs* 31:302-309, 2008; quiz 310-311
23. Schulze T, Mucke J, Markwardt J, et al: Long-term morbidity of patients with early breast cancer after sentinel lymph node biopsy compared to axillary lymph node dissection. *J Surg Oncol* 93:109-119, 2006
24. Velloso FS, Barra AA, Dias RC: Functional performance of upper limb and quality of life after sentinel lymph node biopsy of breast cancer. *Rev Bras Fisioter* 15:146-153, 2011
25. Wilke LG, McCall LM, Posther KE, et al: Surgical complications associated with sentinel lymph node biopsy: Results from a prospective international cooperative group trial. *Ann Surg Oncol* 13:491-500, 2006
26. Gebruers N, Verbelen H, De Vrieze T, et al: Incidence and time path of lymphedema in sentinel node negative breast cancer patients: A systematic review. *Arch Phys Med Rehabil* 96:1131-1139, 2015
27. Giuliano AE, McCall L, Beitsch P, et al: Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: The American College of Surgeons Oncology Group Z0011 randomized trial. *Ann Surg* 252:426-432, 2010; discussion 432-433
28. Boughey JC, Suman VJ, Mittendorf EA, et al: Alliance for Clinical Trials in Oncology: Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer—The ACOSOG Z1071 (Alliance) clinical trial. *JAMA* 310:1455-1461, 2013
29. Cheng CT, Deitch JM, Haines IE, et al: Do medical procedures in the arm increase the risk of lymphoedema after axillary surgery? A review. *ANZ J Surg* 84:510-514, 2014
30. Ferguson CM, Swaroop MN, Horick N, et al: Impact of ipsilateral blood draws, injections, blood pressure measurements, and air travel on the risk of lymphedema for patients treated for breast cancer. *J Clin Oncol* 34:691-698, 2016
31. Cemal Y, Pusic A, Mehrara BJ: Preventative measures for lymphedema: Separating fact from fiction. *J Am Coll Surg* 213:543-551, 2011
32. Kilbreath SL, Ward LC, Lane K, et al: Effect of air travel on lymphedema risk in women with history of breast cancer. *Breast Cancer Res Treat* 120:649-654, 2010
33. Graham PH: Compression prophylaxis may increase the potential for flight-associated lymphoedema after breast cancer treatment. *Breast* 11:66-71, 2002
34. National Lymphedema Network: Position statement of the National Lymphedema Network. Topic: Air travel. <http://www.lymphnet.org/pdfDocs/nlnairtravel.pdf>
35. Box RC, Reul-Hirche HM, Bullock-Saxton JE, et al: Physiotherapy after breast cancer surgery: Results of a randomised controlled study to minimise lymphoedema. *Breast Cancer Res Treat* 75:51-64, 2002
36. Torres Lacomba M, Yuste Sánchez MJ, Zapico Goñi A, et al: Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: Randomised, single blinded, clinical trial. *BMJ* 340:b5396, 2010
37. Thompson M, Korourian S, Henry-Tillman R, et al: Axillary reverse mapping (ARM): A new concept to identify and enhance lymphatic preservation. *Ann Surg Oncol* 14:1890-1895, 2007
38. Pasko JL, Garreau J, Carl A, et al: Axillary reverse lymphatic mapping reduces patient perceived incidence of lymphedema after axillary dissection in breast cancer. *Am J Surg* 209:890-895, 2015
39. Noguchi M, Miura S, Morioka E, et al: Is axillary reverse mapping feasible in breast cancer patients? *Eur J Surg Oncol* 41:442-449, 2015
40. Feldman S, Bansil H, Ascherman J, et al: Single institution experience with lymphatic microsurgical preventive healing approach (LYMPHA) for the primary prevention of lymphedema. *Ann Surg Oncol* 22:3296-3301, 2015
41. Boccardo FM, Casabona F, Friedman D, et al: Surgical prevention of arm lymphedema after breast cancer treatment. *Ann Surg Oncol* 18:2500-2505, 2011

DOI: 10.1200/JCO.2015.64.9574; published online ahead of print at www.jco.org on December 28, 2015.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Lymphedema Precautions: Time to Abandon Old Practices?

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

Soojin Ahn

No relationship to disclose

Elisa R. Port

Leadership: RF Surgical Systems (I)

Stock or Other Ownership: RF Surgical Systems (I), Angiocrine
Bioscience (I)

Patents, Royalties, Other Intellectual Property: RF Surgical Systems (I)