## Debunking Lymphedema Risk-Reduction Behaviors: Risky Conclusions

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A RECENT ARTICLE IN the *Journal of Clinical Oncology* by Ferguson et al.<sup>1</sup> is being summarized, both in the *NEJM Journal Watch* and in the associated JCO editorial by Ahn and Port,<sup>2</sup> as demonstrating and proving that iatrogenic trauma to the at-risk arm and flying without compression garments do not cause breast cancer-related lymphedema (BCRL), and clinical practice should be changed to reflect these conclusions.<sup>2</sup> *Journal Watch* states: "Study debunks conventional guidance about lymphedema prevention."

A physician or health care provider can now rebut a woman who asks for avoidance of an IV/automatic blood pressure measurement/IM injection that the evidence "proves" she is at no risk. The editorial states that only weight gain and infection are proven to cause BCRL and counsels providers to take blood pressure in the at-risk arm. This places women in a predicament. Women will be at risk from their health care providers who have read the summary of this article, and associated editorial, and now believe that the evidence supports "debunking" lymphedema risk-reduction behaviors. However, a close reading of the article, and knowledge of the disease and literature cited, shows that no such sweeping conclusion can be drawn.

The actual article reported the study limitations and summarized that the "burdensome" risk-reduction guidelines did not appear to increase arm swelling in their patients: a far less sweeping and practice-changing conclusion than Ahn and Port suggest.

Full disclosure: I quite literally have skin in this game. I have BCRL that was triggered by an insect bite. I was given no information on risk reduction and was told I had a 7% chance, and not to worry. I engaged in behaviors that in retrospect led to increased trauma to the lymphatics in my at-risk arm. And although I no longer require treatment for breast cancer, I must treat my lymphedema every day to control it.

Quality of life in breast cancer survivors is profoundly impaired by lymphedema.<sup>3,4</sup> Health care providers are ill informed about the disease, and rarely screen for it in survivors. And although the onset is typically in the first few years after treatment, the risk is life-long.<sup>5</sup>

Lymphedema has no objective universal diagnostic criteria.<sup>5,6</sup> It is a clinical diagnosis, swelling is only one aspect of the diagnosis, and it may be present without measurable swelling. The perometer used in this study only measures the increase in arm volume above the wrists and cannot measure swelling in the hand or chest. It cannot measure subclinical lymphedema without measurable swelling. It is not a standalone tool for measuring lymphedema and cannot ascertain volume increases in the entire quadrant at risk. Lymphedema is not a static disease, and those women with fluctuating swelling and swelling in the hands, trunks, or breasts will be missed by the perometer. The greatest yield in diagnosis comes from careful observation, surveys, and volume measurement.<sup>5,7</sup> The editorial dismissed surveys as subjective, yet Armer et al. and others have found surveys to be both validated and highly correlated with BCRL.

Ferguson et al. presented an observational study, which has limitations. The patients' arm volumes were used to determine whether they had lymphedema. The authors were careful to state that they only measured arm volume, but implied that the 10% increase was synonymous with BCRL. This perometry criterion will not diagnose lymphedema in patients with subtle changes, variable changes, and lymphedema in the hand, breast, or trunk. The conclusion was that blood draws, injections, blood pressure readings, and air travel "may not" be associated with arm volume increases. This is a very narrow finding and not a definitive conclusion. Unfortunately, the associated editorial and the *Journal Watch* summaries have extrapolated this conclusion to support the debunking of lymphedema risk-reduction behaviors.

The authors do agree that patients with similar characteristics vary in their rates of developing lymphedema, but rather than postulate that genetic predisposition, periods of increased risk to the lymphatic system, and treatment variations—surgical technique, radiation planning, chemotherapeutic agents, and aging—might be responsible for this variable risk of lymphedema; they focus only on iatrogenic trauma to the at-risk arm and air travel without compression.

The authors define lymphedema as a 10% volume increase of the arm. This definition of lymphedema is not a universal standard: none exists. Stout used 3% volume increase to indicate lymphedema,<sup>8</sup> the Clinical Resource Efficiency Support Team (CREST) criteria have used 5%.<sup>9</sup> In studies using a 10% volume increase, combined with clinician assessment, 5% of patients had the volume increase, whereas 31% were identified by examination.<sup>7</sup>

Patients had a baseline measurement, a postoperative measurement, and at least one 6-month measurement. They completed a survey—recall bias was inherent in the study.

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## LYMPHEDEMA RISK REDUCTION HAS NOT BEEN DEBUNKED

Most patients had avoided trauma to the arm, so only 2.1% had had an injection, only 8.5% a blood draw, and no woman who wore a compression garment while flying was allowed to be included in the analysis.<sup>1</sup>

The authors conclude that although their study suffers from recall bias and short follow-up, they cannot "affirmatively state that risk-reduction practices have no effect on arm swelling," but they hope to bring reasonable doubt to "burdensome guidelines."

The editorial reported a case where a violinist was counseled to avoid compression with air flight and has remained free from lymphedema. This was extrapolated to show how burdensome risk-reduction behaviors are unnecessary.

In the editorial, "Time to Abandon Old Practices?" the risk of BRCL after sentinel node biopsy (SNB) was reported at 5%, yet other data report that risk at 25% when whole breast radiation is included, as it radiates the level I/II nodes. As noted in the editorial, with no standard diagnostic criterion, incidence guidelines will vary—considerably.<sup>5</sup> Lymphedema is a clinical diagnosis, but as "we are addicted to objectification and parameterization in medicine so it never seems to stick."<sup>10</sup>

The editorial described the article in question was as a "rigorous, prospective trial," rather than an observational trial, with exclusion of women who wore compression garments during air travel, and a definition of arm volume increase of 10% as synonymous with BCRL. And although a large number of women were followed, very few recalled having experienced "risky" behavior in their arms.

The editorial concludes, "only weight gain and infections have been shown to be true risk factors in developing lymphedema." This is a vast over simplification, as radiation, genetic predisposition, surgical technique, and biomarkers have all been shown to be risk factors in developing lymphedema.

The table included in the editorial reports that patients should continue to get blood pressure measurements in their at-risk arms, whereas the article's conclusion is only that obtaining a blood pressure in the at-risk arm might not be associated with increased arm swelling in the period that their patients were measured.

Clinicians reading this editorial can now place an automated cuff on a patient and state that the evidence supports that it will never cause or trigger the onset of BCRL, yet the evidence presented in the article does not support this practice alteration. The degree of medical invasiveness varies, and the Ferguson article and accompanying editorial do not differentiate a manual blood pressure reading from repetitive automated readings.

Use of compression garments while flying excluded women from the Ferguson trial analysis. The topic is controversial for women at risk. Unfortunately the data to conclude that air flight presents a risk for the onset of BCRL do not have solid clinical data to support the risk. The editorial cited Graham, a study where a single surgeon queried his patients, and performed two-point measurements and concluded that flights of fewer than 4.5 hours might be safe. This is poor quality evidence, and should not support clinical practice.<sup>11</sup>

Lymphedema is not simply swelling, and Ferguson et al. carefully omitted stating that risk-reduction behaviors induced lymphedema, but rather did not appear to cause "arm swelling." The accompanying editorial drew a far more sweeping and concerning conclusion, and recommended that routine blood pressure monitoring in the at-risk arm should be standard medical practice.

Lymphedema is an inflammatory condition, a disruption of the immune system, and the greatest risk for progressive lymphedema is mild lymphedema. BCRL is under diagnosed and under treated. It has profound impacts on the health and quality of life of breast cancer survivors.<sup>5</sup> Medical treatment has moved toward reducing the risk by reducing the extent of axillary clearance and actually proposing that lymph node staging may be unnecessary in clinically node-negative patients.<sup>12,13</sup>

Is avoidance of medical trauma to an at-risk limb burdensome? Is an incurable condition worthy of minor alterations in medical treatment? Should patient counseling avoid over-simplification and explain the extent of our current knowledge as well as our knowledge deficits? Are riskreduction behaviors more burdensome for health care providers than patients?

Education on risk reduction has been found to reduce the incidence of lymphedema.

The Ferguson article narrowly showed that self-reported risk behaviors, which represented a small minority of women, did not cause arm swelling in the period of their monitoring. It concluded that further research was warranted. The editorial concluded that only obesity and cellulitis cause BCRL, and the current risk-reduction behaviors are never warranted. The latter conclusion is neither supported by the literature nor by the article that was reviewed.

This "debunking" has the potential to harm, and is not supported by the literature. Clinicians who quickly scanned their Journal Watch or read the editorial could possibly counsel women that their requests to avoid iatrogenic harm to their at-risk arms are unnecessary, and rather than allowing women to make an informed decision and supporting that decision, they will traumatize their at-risk arms in high pressure automated blood pressure cuffs and with IM and IV injections, and tell women that their concerns are meritless. Despite tremendous clinical evidence that air flight might trigger lymphedema, clinicians will not assess and inform women based on their individual risk but counsel them, based on poor-quality studies, that there is no risk. Even Graham, who simply queried patients and took inadequate measurements, concluded: "this is not to say that there is no risk, or no women at risk, or that swelling never occurs."<sup>11</sup>

Risk for lymphedema is multifactorial and women should be given accurate counsel and supported in their decisions. This need to debunk risk reduction does not relieve women of burdensome guidelines, but over simplifies, puts them in harm's way, and denies their reality of their risk of lymphedema and prudent steps they can take to avoid this risk. Debunking prohibits truly informed decision making by patients and providers.

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