Breast cancer-associated lymphedema

AUTHOR: Babak Mehrara, MD
SECTION EDITORS: Daniel F Hayes, MD, Larissa Nekhlyudov, MD, MPH, Eduardo Bruera, MD, Patricia A Ganz, MD
DEPUTY EDITORS: Kathryn A Collins, MD, PhD, FACS, Sadhna R Vora, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Apr 26, 2022.**

INTRODUCTION

Lymphedema is defined as the interstitial collection of protein-rich fluid due to disruption of lymphatic flow. Lymphedema occurs when the lymphatic load exceeds the transport capacity of the lymphatic system, which causes filtered fluid to accumulate [1]. Lymphedema that occurs as the result of disease or treatments is called secondary lymphedema. Treatment of breast cancer (eg, surgery, radiation therapy) is one of the most common causes of secondary peripheral lymphedema. Surgical removal of lymph nodes (lymphadenectomy) and radiation therapy are the main cause of lymphedema in patients with breast cancer, but breast cancer-associated lymphedema (BCAL) can also occur due to obstruction of the lymphatic channels or lymph nodes, or infiltration with tumor cells (lymphangitic carcinomatosis).

Upper extremity lymphedema occurring in breast cancer patients, including risk factors, monitoring, prevention, and efficacy of lymphedema treatments, will be reviewed here. General considerations for the diagnosis and management of lymphedema that includes other etiologies, and surgical treatment of lymphedema, are reviewed elsewhere. (See "Clinical features and diagnosis of peripheral lymphedema" and "Clinical staging and conservative management of peripheral lymphedema" and "Surgical treatment of primary and secondary lymphedema".)

ANATOMY

In the upper extremity and chest wall, the superficial lymphatic system (lymphatic capillaries and precollectors) drains interstitial fluid from the skin and subcutaneous tissue into larger collecting vessels (ie, deep lymphatics). The deep lymphatics drain into the axillary lymph nodes where foreign material is filtered and where antigen-presenting cells interact with T and B cells to activate immune responses [1]. The lymphatics of the breast drain into the internal mammary nodes medially, and the axillary and supraclavicular nodes laterally and superiorly (figure 1). The lymph draining from the left upper body (upper extremity, chest wall, upper back, shoulder, and breast) enters the venous circulation through the thoracic duct, which opens into the venous angle between the left subclavian vein and left internal jugular vein (figure 2) [1]. The lymph draining from the right upper body drains into the right venous angle via the right lymphatic duct.

INCIDENCE AND RISK FACTORS

Breast cancer and its associated treatments are one of the most common causes of upper extremity lymphedema. In a systematic review that included 72 studies (29,612 women), the overall incidence of arm lymphedema in breast cancer survivors was 17 percent [2]. The incidence varied based on the mode of diagnosis; it was 13, 15, and 20 percent based on clinical information, formal measurement (eg, arm circumference), and self-assessment, respectively. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Diagnosis'.)

Risk factors — The main risk factors for breast cancer-associated lymphedema (BCAL) include invasive cancer diagnosis, dissection/disruption of axillary lymph nodes, radiation therapy, local infection, and obesity, but other factors may also contribute [3-5].

Axillary reverse mapping (ARM) may reduce the risk for lymphedema in patients undergoing sentinel lymph node biopsy or axillary lymph node dissection [6]. The manner and timing of breast reconstruction may also play a role in the development of lymphedema [7]. (See "Technique of axillary lymph node dissection", section on 'Axillary reverse mapping' and "Overview of breast reconstruction".)

Axillary node dissection — Lymphadenectomy is the primary cause of breast and upper extremity lymphedema in patients with breast cancer [1,2,4,8-14]. The incidence of lymphedema increases with increasing number of axillary nodes removed or disrupted [15]. In a systematic review, the incidence of lymphedema was approximately four times higher in women who had an axillary lymph node dissection compared with those who had sentinel node biopsy (19.9 versus 5.6 percent) [2]. Among patients who have undergone complete axillary node dissection, in one review, lymphedema developed in 23 percent when measured using

limb volume and 45 percent using bioimpedance spectroscopy criteria [4]. Fortunately, contemporary surgical treatment of breast cancer does not automatically mandate axillary node dissection in women with clinically node-negative axilla. Instead, most women undergo sentinel lymph node biopsy, which is associated with a significantly lower risk of lymphedema compared with axillary node dissection (odds ratio [OR] 0.36, 95% CI 0.15-0.86) [16]. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Cancer and cancer treatment' and "Overview of management of the regional lymph nodes in breast cancer" and "Overview of sentinel lymph node biopsy in breast cancer".)

Radiation therapy — Postoperative radiation therapy (breast, axilla, supraclavicular region) also increases the risk for lymphedema [17-22]. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer".)

In a systematic review, the incidence of lymphedema was significantly higher among women who underwent surgery plus radiation therapy compared with surgery alone (41 versus 17 percent) [20]. Among women who have undergone axillary node dissection, radiation therapy is an additive risk factor. In one report, the incidence of subjective lymphedema with axillary node dissection alone and axillary node dissection plus radiation therapy were 7 and 38 percent, respectively [22].

Women undergoing breast-conserving therapy are also at risk for lymphedema following adjuvant radiation therapy [18,20]. A retrospective study involved 1497 women treated for breast cancer between 1980 and 2006 (75 percent with node-negative breast cancer) [18]. For the entire cohort, the reported incidence of lymphedema was 7 percent. For women treated with supraclavicular, axillary, or internal mammary radiation therapy, the incidences of lymphedema were 10, 15, and 8 percent, respectively.

Variations in the radiation therapy field design may impact the development of lymphedema. A retrospective study of 492 women treated for breast cancer showed that inclusion of level I and II axillary lymph nodes in the radiation field (ie, the radiation field included more than one third of the humoral head) significantly increased the risk of developing breast cancer-related lymphedema compared with patients in whom this area was excluded [23]. Women treated in this manner had a significantly greater increase in the incidence of lymphedema (37.1 versus 7.7 percent).

Other factors — Beyond lymphadenectomy and radiation therapy, the likelihood of developing lymphedema is related to increased body mass index or obesity [17,24]; postoperative infection, hematoma, or seroma; and possibly medication effects (eg, taxanes [25], longer duration of chemotherapy [26]). Weight gain is a contributory factor to the

development of lymphedema [27]; obesity alone may impair lymphatic function and lead to the development of lymphedema [28]. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Obesity'.)

CLINICAL FEATURES, DIAGNOSIS, AND STAGING

Typical signs and symptoms of lymphedema include progressive upper extremity swelling, skin changes, limb pain and discomfort, restricted range of motion, and nonpitting edema. Restricted range of motion can be associated with the presence of thickened bands or cord of tissue [29]. Superficial phlebitis of the chest wall veins (Mondor disease) has also been associated with upper extremity lymphedema. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Clinical features'.)

Physical findings of asymmetric upper extremity measurements can usually establish a diagnosis of lymphedema. Methods to obtain clinical measurements are reviewed separately. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Diagnosis'.)

The differential diagnosis of lymphedema in patients with breast cancer includes other conditions associated with peripheral edema. Deep vein thrombosis related to central venous access is an important cause of upper extremity edema. Although central access is usually contralateral to the side of the breast surgery, particularly if there has been an axillary node dissection or axillary radiation, ipsilateral deep vein thrombosis can still occur. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Differential diagnosis' and "Catheter-related upper extremity venous thrombosis in adults".)

An onset of lymphedema several years after the primary surgery without obvious trauma should raise suspicion for tumor, which always needs to be evaluated. In particular, recurrence of the breast cancer in the axillary area or the development of lymphangiosarcoma should be excluded with breast imaging [30-32]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Lymphangiosarcoma'.)

Clinical staging — Lymphedema is staged (International Society of Lymphology) based on the examination of the upper extremity and the volume difference between the extremities as stage 0 through stage III, which correspond to subclinical lymphedema, mild lymphedema, moderate lymphedema, and severe lymphedema [33]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Clinical stage'.)

NATURAL HISTORY AND MONITORING

Following treatment for breast cancer, the onset of lymphedema is insidious and is typically characterized by slowly progressive swelling of the upper extremity ipsilateral to the axillary node dissection or radiation treatments [34].

At first, the swelling may be apparent only in the proximal portion of the limb, or it can affect only a portion of the distal limb including the digits. There may also be swelling over the ipsilateral breast and/or upper chest wall. In one systematic review, the greatest risk for developing upper extremity lymphedema was within the first two years following diagnosis and treatment [2]. However, the type of treatment appears to influence time course, and later onset can occur. In a study of over 2100 women who received surgery for breast cancer, early-onset lymphedema (<12 months postoperatively) was associated with axillary lymph node dissection (hazard ratio [HR] 4.8, 95% CI 2.6-8.8), while late-onset lymphedema (>12 months postoperatively) was associated with regional lymph node radiation (HR 3.9, 95% CI 2.0-7.4) and, to a lesser extent, axillary lymph node dissection (HR 1.9, 95% CI 1.1-3.2) [35]. The lymphedema risk peaked between 6 and 12 months in the axillary dissection **without** regional lymph node radiation group, between 18 and 24 months in the axillary dissection **with** regional lymph node radiation group, and between 36 and 48 months in the group receiving sentinel lymph node biopsy **with** regional lymph node radiation. On multivariate analysis, body mass index was also associated with lymphedema.

Early identification of those at risk for lymphedema (ISL stage 0) and protection measures in those with lymphedema (ISL stages I, II, III) may potentially keep lymphedema from progressing to a higher clinical stage; lymphedema is often difficult to treat if it progresses [36,37]. In a case-control study of 196 breast cancer patients, the application of a surveillance program that included preoperative limb volume measurement and interval postoperative follow-up was able to detect subclinical lymphedema (defined as a 3 percent difference in arm circumference), reduce affected limb volume with early treatment (with a compression sleeve and gauntlet), and maintain this volume reduction [38].

Measurements of arm circumference and/or volume are common methods for monitoring the onset and degree of lymphedema [4,33,39-41]. Other methods, such as measurements of bioimpedance spectroscopy, tissue compression (tonometry), and local tissue water, have also been investigated [42-45]. Clinical measurements are obtained initially to establish a baseline before breast cancer treatments and afterward at intervals to track changes during treatment. Alternatively, changes in arm circumference or volume relative to the contralateral normal limb can be performed. There is currently no consensus on how frequently these measurements should be performed, nor on the frequency of follow-up of women at risk for developing lymphedema. However, given that the highest risk of developing lymphedema is within the first

three years of treatment and that early intervention can limit progression of disease, high-risk patients should be followed closely in this period (eg, every six months or if they develop symptoms). In addition, patients should be taught how to self-monitor. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Extremity measurements' and 'Primary prevention' below.)

PRIMARY PREVENTION

Primary prevention strategies aim to avoid the occurrence of lymphedema and promote patient well-being. For women with breast cancer, the only measure that effectively reduces the risk of developing lymphedema involves using sentinel lymph node biopsy for axillary lymph node staging rather than axillary node dissection. The role of lymph node reconstruction is under active investigation [46].

Breast cancer patients should monitor the ipsilateral limb, and among those with risk factors for lymphedema but without limb swelling (ie, ISL stage 0), other measures such as exercise/physiotherapy and compression therapy can be implemented early. However, these measures have not definitively been shown to prevent the occurrence of lymphedema at a later timeframe. (See 'Natural history and monitoring' above and 'Exercise, physiotherapy and compression' below.)

Blood pressure measurement, venipuncture, and peripheral intravenous line placement in the ipsilateral arm not affected by lymphedema has not been shown to affect the occurrence of lymphedema [46,47]. (See 'Risk factors' above and 'Unsupported risk reduction strategies' below.)

Limiting lymph node dissection — Limiting the extent of lymph node removal is the only measure shown to reduce the incidence of breast-cancer associated lymphedema. The use of axillary staging with sentinel node biopsy has reduced the number of axillary lymph node dissections performed and, consequently, the incidence of lymphedema [36]. Clinically relevant lymphedema occurs in 5 to 9 percent of patients who undergo sentinel node biopsy alone compared with approximately 40 percent in patients undergoing axillary lymph node dissection [2,48-51]. (See "Overview of sentinel lymph node biopsy in breast cancer".)

When lymph node dissection is necessary, other surgical techniques may also be effective for primary prevention, including minimizing the extent of lymph node dissection, reverse mapping, and lymphatic bypass [52-54]. Using advanced radiation therapy (RT) techniques that limit radiation may also be helpful.

Lymphatic reconstruction — Lymphovenous bypass (referred to as lymphatic microsurgical preventing healing approach [LYMPHA] or immediate lymphatic reconstruction [ILR]) can also be performed at the time of lymph node dissection to help prevent lymphedema [55]. In the largest series of 74 patients with an average follow-up of four years, only 4 percent of patients treated with LYMPHA developed lymphedema compared with historical rates of 15 to 65 percent [56]. Several centers have ongoing studies attempting to confirm the validity of these findings. (See "Surgical treatment of primary and secondary lymphedema".)

Exercise, physiotherapy and compression — Following treatment of breast cancer, range of motion exercises and compression sleeves are generally recommended for the affected arm [33,46,57-61]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'At risk for postoperative lymphedema'.)

Once any wounds have healed and provided there are no surgical complications that may interfere (eg, need for a drain), exercise and weight training should be encouraged. Properly fitted compression garments should be worn during exercise, including aerobic and resistance training. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Diet and exercise' and 'Compression therapy' below.)

For patients treated by axillary lymph node dissection, some trials, but not all, have supported physiotherapy (with or without manual lymphatic drainage) to improve arm mobility and potentially to prevent lymphedema [61-69].

- In one trial, 116 women with unilateral axillary lymph node dissection were randomly assigned to education, early physiotherapy, and progressive active and action-assisted shoulder exercises, or to education alone [63]. After 12 months of follow-up, significantly fewer women treated with prophylactic physiotherapy developed lymphedema (7 versus 25 percent with education alone).

- In another trial involving 67 women who underwent surgery for breast cancer, patients were randomly assigned to a six-month course of physiotherapy starting on postoperative day 2, or no physiotherapy [68]. At the six-month postoperative reassessment, there was no increase in arm volume among women who underwent physiotherapy; women who did not undergo physiotherapy had a significant increase in upper extremity volume.

- By contrast, in a trial that randomly assigned 158 patients age 18 to 75 years to progressive resistance training (early supervised/later unsupervised) or usual care, arm volume or lymphedema incidence at one year were not significantly different between the groups [69].

Unsupported risk reduction strategies — Other measures have commonly been used in postoperative patients who do **not** exhibit lymphedema (ie, ISL stage 0), but which have not been shown to alter the development of lymphedema or complications following breast cancer surgery. These include avoiding intravenous catheter placement, venipuncture, and blood pressure measurements in the ipsilateral extremity [70,71]. This issue remains a significant concern in the anesthetic management of patients with breast cancer undergoing intervention. While the International Society of Lymphology noted that "while some precautions rest on solid physiological principles (eg, avoiding excessive heat on an at risk limb, not having chemotherapy administered into the limb unless medically necessary), others are less supported" [33]. In agreement with the American Society of Breast Surgeons [46], the Society for Ambulatory Anesthesia (SAMBA) issued a statement that intravenous catheter placement, venipuncture, and blood pressure measurements in the ipsilateral upper extremity are not contraindicated after breast surgery in patients who do not have lymphedema [47]. When fluid therapy and monitoring are required, we support a shared decision-making approach that accounts for the risk of developing lymphedema (lymph node dissection versus sentinel lymph node biopsy, radiation), the clinical situation and monitoring needs (eg, outpatient versus intensive care unit management), and patient preferences. When given a choice, many patients elect to use the contralateral arm [46].

Our approach is as follows:

- For patients without significant risk factors for lymphedema (see 'Risk factors' above) and who do **not** have lymphedema, there is no need to avoid the ipsilateral extremity for intravenous catheter placement, venipuncture, and blood pressure measurements. One study prospectively investigated the association between factors thought to increase the risk for lymphedema in 632 patients treated for breast cancer and screened routinely for lymphedema [72]. On multivariate analysis, there was no significant association between increases in arm volume and blood pressure readings. Significant factors associated with the development of lymphedema included body mass index ≥25, axillary lymph node dissection, regional lymph node irradiation, and cellulitis. There was also no association between blood pressure readings on the ipsilateral arm and cellulitis.

- Whether to avoid ipsilateral blood pressure measurement, venipuncture, and peripheral intravenous line placement in patients with significant risk factors for the development of lymphedema (see 'Risk factors' above) but who do **not** have lymphedema is controversial. We prefer not to use the ipsilateral extremity when another option is available.

LYMPHEDEMA MANAGEMENT

Protection of the affected extremity — For patients with lymphedema, ongoing monitoring and measures to protect the extremity are aimed at minimizing the degree of edema, slowing the rate of lymphedema progression, and preventing complications [62,71,73-76]. These are listed below and reviewed in more detail elsewhere. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'General measures'.)

Patients with lymphedema should be encouraged to:

- Monitor their extremity, including taking upper limb measurements. Measurements should be taken at the metacarpal-phalangeal joints (if edematous), around the wrist, 10 cm below to the olecranon process, and 10 cm above to the olecranon process. The patient should report any changes in size, sensation, color, temperature, or skin condition. In a review of 100 women, perceived swelling and differences in tissue texture between the arm was associated with, and sensitive to, bioimpedance spectroscopy-detected lymphedema [77]. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Extremity measurements' and 'Natural history and monitoring' above.)

- Maintain meticulous skin hygiene and nail care to prevent a portal of entry for infection that may result in cellulitis. Use skin moisturizers and treat small breaks in the skin, as may be induced by a paper cut or abrasions, pinpricks, insect bites, or pet scratches, with topical antibiotics. Protect exposed skin using sunscreen and wear gloves when participating in activities that could lead to skin injury.

- Seek medical attention and treatment for any clinical signs that could represent an episodes of cellulitis. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

- Elevate the extremity when able. Simple elevation may reduce swelling, particularly in the early stage of lymphedema [78].

- Continue to exercise. Upper body exercise is safe in women treated by axillary lymph node dissection [63,68,69,79-92]. In a systematic review, a significant reduction of lymphedema was documented by bioimpedance spectroscopy values in response to resistance exercise [58].

- Wear properly fitted graded compression sleeves, which can reduce the degree of lymphedema. (See 'Compression therapy' below.)

- Avoid procedures that puncture the skin of the lymphedematous arm (eg, vaccination, acupuncture, phlebotomy, intravenous lines, venography). When needed, these can be

performed in the contralateral arm [93]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Avoid skin infection/injury'.)

- Maintain ideal body weight [37]. In addition to increasing the risk for breast-cancer associated lymphedema, obesity may also limit the effectiveness of compression pumps or sleeves.

Blood pressure measurement — For patients with lymphedema (ie, ISL stage I, II, III), we support a recommendation to measure blood pressure in the contralateral arm, particularly in any setting in which blood pressure is being closely repeatedly or continuously monitored (eg, in an intensive care unit, recovery room, or during procedures). This recommendation is based upon several factors. Blood pressure measurement in an enlarged extremity will be inaccurate if the cuff is not properly sized and the cuff causes a high-pressure focal compression (in contrast to pneumatic compression devices used for lymphedema treatment, for which the compression is applied sequentially) [70,71]. Among the rare patient who has undergone bilateral axillary lymph node dissection and has bilateral lymphedema, routine blood pressure measurements can be obtained in the lower extremity. If the patient has had bilateral axillary lymph node dissection and there is not an option of obtaining blood pressure measurements in the lower extremity, then a manual (but not automatic) blood pressure cuff can be used intermittently, but inflated to only just above the expected level of systolic blood pressure [70]. (See "Blood pressure measurement in the diagnosis and management of hypertension in adults", section on 'Leg blood pressure'.)

Care during travel — Although in theory lymphedema may be exacerbated at high altitude or during air travel, since the ambient atmosphere pressure is less than the relative outlet transcapillary pressure within the superficial tissues, studies suggest that the risk from air travel of precipitating or worsening lymphedema is low [94-96]. The use of compression sleeves during air flight in women with lymphedema is debated. Some suggest that domestic air travel (<4.5 hours) is low risk and that compression devices may be counterproductive [97]. For longer-duration air travel, compression garments, exercises, and self-massage may all be helpful. (See 'Compression therapy' below.)

Effectiveness of conservative treatments — Untreated, the degree of lymphedema increases over time [98]. Early, consistent, and ongoing treatment is necessary to limit the amount of extremity swelling. The conservative treatment of established lymphedema consists of a multimodality regimen that includes general self-care measures (exercise, skin care), compression therapy (compression bandaging, compression garments, intermittent pneumatic compression), and physiotherapy (eg, simple lymphatic drainage, manual lymphatic drainage, complete decongestive therapy), the type and the intensity of which depend upon the clinical

stage [33,46,99-101]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Conservative treatment by severity'.)

The effectiveness of these treatments in patients with established breast cancer-associated lymphedema (BCAL) is summarized below.

- For patients with mild lymphedema (ISL stage I), we suggest physiotherapy in the form of manual lymphatic drainage and compression garments, rather than more intensive therapy. Manual lymphatic drainage (MLD) is a massage-like technique that is typically performed by specially trained physical therapists, but a self-help maneuver (simple lymphatic drainage) has also been used for mild cases. Light pressure is used to mobilize edema fluid from distal to proximal areas. (See 'Manual lymphatic drainage' below.)

- For patients with moderate-to-severe lymphedema (ISL stages II to III) and no contraindications, we suggest intensive physiotherapy, usually in the form of complete decongestive therapy, rather than less intense therapy. Complete decongestive therapy (CDT) refers to a two-phase (treatment phase, maintenance phase) multicomponent technique that is designed to reduce the degree of lymphedema and to maintain the health of the skin and supporting structures. (See 'Complete decongestive therapy' below.)

- Patients with severe lymphedema (ISL stage III) may also benefit from intermittent pneumatic compression (IPC) in addition to CDT. IPC (also called sequential pneumatic compression) devices employ a plastic sleeve or stocking that is intermittently inflated over the affected limb. Most pneumatic compression pumps sequentially inflate a series of chambers in a distal-to-proximal direction. (See 'Intermittent pneumatic compression' below.)

Compression therapy — Compression therapy, often combined with physiotherapy in the form of manual lymphatic drainage (MLD), is used in the initial stages of lymphedema management. Limb compression uses multilayered padding materials and short-stretch (also called low-stretch) bandages. Maintenance therapy uses fitted compression garments (at least class I compression) worn during waking hours. A compression hand piece, either a glove or a gauntlet, is necessary when wearing a compression sleeve to prevent swelling in the hand. When correctly fitted and worn properly, compression garments can help reduce swelling; however, poorly fitted garments can be restrictive and can exacerbate lymphedema. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Compression therapy'.)

Compression garments and compression bandaging are effective for reducing limb lymphedema volume. Reported percentage reductions with compression garments or

compression bandaging among various etiologies of lymphedema range from 17 to 60 percent [102]. In a randomized trial in 307 women who had undergone axillary lymph node dissection for breast cancer, those assigned to compression therapy developed arm swelling less frequently compared with the control group (14 versus 25 percent, as measured by relative arm volume increase) [57]. A separate trial randomly assigned 90 women with unilateral lymphedema to multilayered short-stretch bandaging for 18 days followed by elastic hosiery for 24 weeks with elastic hosiery alone for 24 weeks [103]. Combined therapy was approximately twice as effective in reducing limb volume (31 versus 16 percent at 24 weeks).

Manual lymphatic drainage — Manual lymphatic drainage (MLD) appears to offer an additional benefit to compression therapy for swelling reduction in patients with BCAL, particularly for those with mild-to-moderate lymphedema [104,105]. MLD is a massage-like technique that is performed by specially trained physical therapists [1]. MLD is also a component of complete decongestive therapy. (See 'Complete decongestive therapy' below.).

MLD and contraindications are described separately. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Manual lymphatic drainage' and "Clinical staging and conservative management of peripheral lymphedema", section on 'Contraindications'.)

Support for MLD in women with BCAL comes from both observational studies [106-109] and small randomized trials [63,104,110-112]. A systematic review that included six trials [104,110-112] concluded that MLD is safe and noted that MLD may offer additional benefit to compression bandaging for reducing swelling, more so for women with mild-to-moderate breast cancer-related lymphedema as compared with moderate-to-severe lymphedema [105]. In one of these trials with 31 women with BCAL, the reduction in excess volume and dermal thickness in the arm treated with MLD was greater compared with simple lymphatic drainage (SLD; a commonly taught self-help maneuver) [110]. MLD also significantly improved several quality-of-life domains, including emotional function, occurrence of dyspnea, and disturbances in sleep. It should be noted that not all studies have found a benefit for MLD. As an example, in one trial, 42 women with lymphedema were randomly assigned to standard therapy (compression garments, physical exercises, and education) with or without a short course of MLD (eight sessions in two weeks) [113]. After a follow-up of 12 months, both groups had a similar reduction in arm volume, suggesting that MLD had little impact over standard management.

Complete decongestive therapy — Complete decongestive therapy (CDT) is a multicomponent technique designed to reduce the severity of lymphedema and maintain the health of the skin and supporting structures [1]. For patients with moderate-to-severe

lymphedema following treatment for breast cancer, CDT is recommended as a component of a multimodality regimen for the treatment of lymphedema [1]. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Complete decongestive therapy'.)

The effectiveness of CDT in women with breast cancer associated lymphoma is suggested in observational studies [114], which demonstrated a reduction in limb volume with improved pain, cosmesis, and/or function [106,115-126]. In these studies, reductions in limb volume range from 30 to 70 percent. However, patient compliance is required for long-term success. In one study, at least 90 percent of the lymphedema reduction was maintained in compliant patients at an average follow-up of nine months, while noncompliant patients lost approximately one third of the initial benefit [115]. Small randomized trials in patients with BCAL have mixed results [127-129].

In a small phase trial, 53 patients with BCAL were randomly assigned to CDT (lymph drainage, multilayer compression bandaging, elevation, remedial exercise, and skin care) or standard physiotherapy (bandages, elevation, head-neck and shoulder exercises, and skin care) [129]. The group receiving CDT had a significantly greater improvement in edema as measured by circumferential and volumetric measurements. A separate trial suggested minimal benefit for CDT over compression garments as a first-line treatment of lymphedema. In this trial, 95 patients with BCAL were randomly assigned to CDT or compression garments alone [128]. A greater absolute reduction in arm volume was seen for CDT compared with compression garments (250 versus 142 mL), but the mean reduction in arm volume was not significantly different (29 versus 23 percent). There were no differences in severe adverse events. Several factors may limit the applicability of the findings of these trials. The trial was small and may lack sufficient power to detect a significant volume difference. Also, the study excluded patients who had not responded to conservative strategies (eg, compression garments or bandaging). However, another small trial involving 52 patients with BCAL following mastectomy also found no significant difference in relative volume change for CDT compared with compression [127].

Intermittent pneumatic compression — Intermittent pneumatic compression (IPC; also called sequential pneumatic compression) is another method of compression therapy for patients with typically severe lymphedema. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Intermittent pneumatic compression'.)

A number of studies have evaluated the role of IPC in patients with lymphedema following breast cancer treatment [107,112,125,130-136]. A systematic review of IPC in patients with BCAL identified seven trials [137]. Among three trials that reported volume reductions [125,130,133], there were no significant differences between routine management of lymphedema with and

without the use of IPC. On the other hand, IPC may still be an effective addition to a multimodality lymphedema treatment regimen. One of these trials randomly assigned 23 patients with unilateral previously untreated BCAL to CDT alone or with adjunctive IPC (30 minutes daily for 10 days) [125]. A significantly greater reduction in limb volume during initial treatment was seen for combined therapy compared with CDT alone (45 versus 26 percent). A second arm of the trial evaluated the efficacy of maintenance IPC therapy (self-administered 60 minutes daily) added to CDT in 27 patients with unilateral breast cancer-associated lymphedema who had previously been treated with CDT [125]. At 6 to 12 months, a fall in mean limb volume occurred with combined therapy compared with an increase with CDT alone (-90 versus +33 mL), a difference that was statistically significant.

In addition to the paucity of data demonstrating benefit from IPC in women with BCAL, there are a number of concerns:

- The ideal pressure for the pump is not known, and some investigators suggest that a pressure greater than 60 mmHg may injure lymphatic vessels.
- IPC is usually applied daily or five times per week. However, the optimal duration of IPC is not known, as in different studies, the sessions have varied in length (90 minutes to as long as 6 hours) and duration (two to three days to four weeks) [103,112,125,131,136].

Thus, IPC may be considered an adjunct in patients who do not respond well to CDT and compression garments. If the lymphedema is controlled with IPC, a gradient pressure garment should be worn to prevent further limb swelling. Clinical experience has shown that IPC may be an alternative maintenance program for lymphedema patients who have difficulty in performing self-MLD secondary to weakness, fatigue, or range of motion deficits. It may also be beneficial for lymphedema patients who are unable to utilize compression bandaging or garments due to skin allergies from the materials used in these compression products.

Surgery — For selected patients with lymphedema or complications related to lymphedema, surgery to help alleviate pain and discomfort and reduce the risk of infection, among other goals, may be reasonable to consider. Surgery is most effective for patients with early-stage lymphedema (ie, prior to tissue fibrosis and severe adipose deposition); however, surgery is also possible and effective in patients with late-stage lymphedema. Techniques include physiologic techniques to improve lymphatic circulation and tissue reduction techniques [138-140]. Techniques are discussed separately. (See "Surgical treatment of primary and secondary lymphedema".)

Palliative care — While compression and physiotherapy are beneficial for extremity lymphedema, their application may be associated with risk (eg, skin breakdown, fluid overload)

when used in the context of metastatic cancer [141]. (See "Overview of comprehensive patient assessment in palliative care".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Lymphedema" and "Society guideline links: Breast surgery".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Peripheral lymphedema after cancer treatment (The Basics)")
- Beyond the Basics topics (see "Patient education: Lymphedema after cancer surgery (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Lymphedema occurs when the load exceeds the transport capacity of the lymphatic system, which leads to the accumulation of protein-rich fluid (lymph) and fibroadipose tissue in the interstitium. Symptoms of lymphedema include limb swelling, skin changes, discomfort, and restricted range of motion. (See 'Introduction' above and 'Anatomy' above

and "Clinical features and diagnosis of peripheral lymphedema", section on 'Clinical features'.)

- Breast cancer and its associated therapies are one of the most common causes of secondary peripheral lymphedema. The incidence of upper extremity lymphedema in breast cancer survivors ranges from 5 to 40 percent depending upon the extent of lymph node disruption and other risk factors such as the presence of obesity or infection. Incidences in the higher range occur in patients who have undergone complete axillary dissection combined with radiation therapy. (See 'Incidence and risk factors' above.)

- Breast cancer-associated lymphedema (BCAL) is primarily due to obstruction of the lymphatic channels located in the axilla, most commonly from lymphadenectomy or radiation therapy, but can also occur as a result of infiltration of the lymphatic vessels by tumor cells (lymphangitic carcinomatosis).

- Primary prevention of lymphedema in patients undergoing treatment for breast cancer relies on surgical techniques that limit node dissection (eg, sentinel lymph node biopsy) or, less commonly, techniques that repair or bypass injured lymphatics, and limiting radiation exposure. Sentinel lymph node biopsy has been instrumental in decreasing the incidence of lymphedema, which occurs in <10 percent of patients who undergo sentinel node biopsy alone. (See 'Primary prevention' above.)

- Monitoring and early identification of lymphedema and initiation of protection measures may help slow progression to a higher clinical stage. These measures are appropriate for all patients with lymphedema. (See 'Natural history and monitoring' above and 'Protection of the affected extremity' above.)

  Patients should be encouraged to:

  - Monitor their extremity, including taking upper limb measurements. Report any changes.
  - Maintain skin and nails to prevent infection or skin injury.
  - Seek medical attention and treatment for any clinical signs of infection.
  - Elevate the extremity, when able.
  - Wear properly fitted graded compression sleeves.
  - Avoid medical procedures that puncture the skin.
  - Maintain ideal body weight.

- Physical findings of asymmetric upper extremity measurements usually establish a diagnosis of lymphedema in at-risk patients. An onset of lymphedema several years after

the primary surgery without obvious trauma should raise suspicion for tumor, in particular, recurrence of the breast cancer in the axillary area or the development of lymphangiosarcoma. (See 'Clinical features, diagnosis, and staging' above.)

- For patients with upper extremity lymphedema, we measure blood pressure in the contralateral arm, particularly in any setting in which blood pressure is being closely monitored (eg, in an intensive care unit, recovery room, or during procedures). Among the rare patient who has undergone bilateral axillary lymph node dissection and has bilateral lymphedema, routine blood pressure measurements can be obtained in the lower extremity. (See 'Blood pressure measurement' above.)

- The conservative treatment of established lymphedema consists of a multimodality regimen that includes general measures for care, physiotherapy (eg, simple lymphatic drainage, manual lymphatic drainage, complete decongestive therapy), and compression therapy (compression bandaging, compression garments, intermittent pneumatic compression), the type and the intensity of which depend upon the clinical stage. The effectiveness of these treatment in patients with BCAL is discussed above. (See 'Effectiveness of conservative treatments' above and "Clinical staging and conservative management of peripheral lymphedema", section on 'Conservative treatment by severity'.)

  - For patients with mild lymphedema (International Society of Lymphology [ISL] stage I), we suggest physiotherapy in the form of manual lymphatic drainage and compression garments, rather than more intensive therapy (**Grade 2B**). Manual lymphatic drainage (MLD) is a massage-like technique that is typically performed by specially trained physical therapists, but a self-help maneuver (simple lymphatic drainage) has also been used for mild cases. Light pressure is used to mobilize edema fluid from distal to proximal areas. (See 'Manual lymphatic drainage' above.)

  - For patients with moderate-to-severe lymphedema (ISL stages II to III) and no contraindications, we suggest intensive physiotherapy, usually in the form of complete decongestive therapy, rather than less intense therapy (**Grade 2B**). Complete decongestive therapy (CDT) refers to a two-phase (treatment phase, maintenance phase) multicomponent technique that is designed to reduce the degree of lymphedema and to maintain the health of the skin and supporting structures. (See 'Complete decongestive therapy' above.)

  - Patients with severe lymphedema (ISL stage III) may also benefit from intermittent pneumatic compression (IPC) in addition to CDT. IPC (also called sequential pneumatic compression) devices employ a plastic sleeve or stocking that is intermittently inflated

over the affected limb. Most pneumatic compression pumps sequentially inflate a series of chambers in a distal-to-proximal direction. (See 'Intermittent pneumatic compression' above.)

- For selected patients with lymphedema or complications related to lymphedema, surgery may be an option with the goals of alleviating pain and discomfort and reducing the risk of infection, among others. Surgery is most effective for patients with early-stage lymphedema (ie, prior to tissue fibrosis and severe adipose deposition); however, surgery is also possible and effective in patients with late-stage lymphedema. (See 'Surgery' above.)

- Complications of lymphedema include skin infections (cellulitis, erysipelas, and lymphangitis), lymphangiosarcoma, and reduced quality of life, including aspects of emotional, functional, physical, and social well-being. (See "Clinical staging and conservative management of peripheral lymphedema", section on 'Complications'.)

ACKNOWLEDGMENT

The editorial staff at UpToDate acknowledge Emile R Mohler, III, MD, now deceased, who contributed to an earlier version of this topic review. UpToDate also acknowledges Dr. Mohler's work as our Section Editor for Vascular Medicine.

REFERENCES

1. Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. CA Cancer J Clin 2009; 59:8.
2. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol 2013; 14:500.
3. McLaughlin SA, Brunelle CL, Taghian A. Breast Cancer-Related Lymphedema: Risk Factors, Screening, Management, and the Impact of Locoregional Treatment. J Clin Oncol 2020; 38:2341.
4. Bundred N, Foden P, Todd C, et al. Increases in arm volume predict lymphoedema and quality of life deficits after axillary surgery: a prospective cohort study. Br J Cancer 2020; 123:17.

5. Basta MN, Wu LC, Kanchwala SK, et al. Reliable prediction of postmastectomy lymphedema: The Risk Assessment Tool Evaluating Lymphedema. Am J Surg 2017; 213:1125.
6. Tummel E, Ochoa D, Korourian S, et al. Does Axillary Reverse Mapping Prevent Lymphedema After Lymphadenectomy? Ann Surg 2017; 265:987.
7. Lee KT, Bang SI, Pyon JK, et al. Method of breast reconstruction and the development of lymphoedema. Br J Surg 2017; 104:230.
8. Naoum GE, Roberts S, Brunelle CL, et al. Quantifying the Impact of Axillary Surgery and Nodal Irradiation on Breast Cancer-Related Lymphedema and Local Tumor Control: Long-Term Results From a Prospective Screening Trial. J Clin Oncol 2020; 38:3430.
9. Hayes SC, Janda M, Cornish B, et al. Lymphedema after breast cancer: incidence, risk factors, and effect on upper body function. J Clin Oncol 2008; 26:3536.
10. Deutsch M, Land S, Begovic M, Sharif S. The incidence of arm edema in women with breast cancer randomized on the National Surgical Adjuvant Breast and Bowel Project study B-04 to radical mastectomy versus total mastectomy and radiotherapy versus total mastectomy alone. Int J Radiat Oncol Biol Phys 2008; 70:1020.
11. Cormier JN, Askew RL, Mungovan KS, et al. Lymphedema beyond breast cancer: a systematic review and meta-analysis of cancer-related secondary lymphedema. Cancer 2010; 116:5138.
12. Rockson SG, Rivera KK. Estimating the population burden of lymphedema. Ann N Y Acad Sci 2008; 1131:147.
13. Boughey JC, Hoskin TL, Cheville AL, et al. Risk factors associated with breast lymphedema. Ann Surg Oncol 2014; 21:1202.
14. Ozaslan C, Kuru B. Lymphedema after treatment of breast cancer. Am J Surg 2004; 187:69.
15. Penn IW, Chang YC, Chuang E, et al. Risk factors and prediction model for persistent breast-cancer-related lymphedema: a 5-year cohort study. Support Care Cancer 2019; 27:991.
16. Purushotham AD, Upponi S, Klevesath MB, et al. Morbidity after sentinel lymph node biopsy in primary breast cancer: results from a randomized controlled trial. J Clin Oncol 2005; 23:4312.
17. Gross JP, Whelan TJ, Parulekar WR, et al. Development and Validation of a Nomogram to Predict Lymphedema After Axillary Surgery and Radiation Therapy in Women With Breast Cancer From the NCIC CTG MA.20 Randomized Trial. Int J Radiat Oncol Biol Phys 2019; 105:165.
18. Shah C, Wilkinson JB, Baschnagel A, et al. Factors associated with the development of breast cancer-related lymphedema after whole-breast irradiation. Int J Radiat Oncol Biol

Phys 2012; 83:1095.

19. Meric F, Buchholz TA, Mirza NQ, et al. Long-term complications associated with breast-conservation surgery and radiotherapy. Ann Surg Oncol 2002; 9:543.
20. Erickson VS, Pearson ML, Ganz PA, et al. Arm edema in breast cancer patients. J Natl Cancer Inst 2001; 93:96.
21. Borup Christensen S, Lundgren E. Sequelae of axillary dissection vs. axillary sampling with or without irradiation for breast cancer. A randomized trial. Acta Chir Scand 1989; 155:515.
22. Kissin MW, Querci della Rovere G, Easton D, Westbury G. Risk of lymphoedema following the treatment of breast cancer. Br J Surg 1986; 73:580.
23. Gross JP, Sachdev S, Helenowski IB, et al. Radiation Therapy Field Design and Lymphedema Risk After Regional Nodal Irradiation for Breast Cancer. Int J Radiat Oncol Biol Phys 2018; 102:71.
24. Helyer LK, Varnic M, Le LW, et al. Obesity is a risk factor for developing postoperative lymphedema in breast cancer patients. Breast J 2010; 16:48.
25. Cariati M, Bains SK, Grootendorst MR, et al. Adjuvant taxanes and the development of breast cancer-related arm lymphoedema. Br J Surg 2015; 102:1071.
26. Armer JM, Ballman KV, McCall L, et al. Factors Associated With Lymphedema in Women With Node-Positive Breast Cancer Treated With Neoadjuvant Chemotherapy and Axillary Dissection. JAMA Surg 2019; 154:800.
27. Eyigör S, Cinar E, Caramat I, Unlu BK. Factors influencing response to lymphedema treatment in patients with breast cancer-related lymphedema. Support Care Cancer 2015; 23:2705.
28. Mehrara BJ, Greene AK. Lymphedema and obesity: is there a link? Plast Reconstr Surg 2014; 134:154e.
29. Brunelle CL, Roberts SA, Shui AM, et al. Patients who report cording after breast cancer surgery are at higher risk of lymphedema: Results from a large prospective screening cohort. J Surg Oncol 2020; 122:155.
30. Stewart FW, Treves N. Classics in oncology: lymphangiosarcoma in postmastectomy lymphedema: a report of six cases in elephantiasis chirurgica. CA Cancer J Clin 1981; 31:284.
31. Tomita K, Yokogawa A, Oda Y, Terahata S. Lymphangiosarcoma in postmastectomy lymphedema (Stewart-Treves syndrome): ultrastructural and immunohistologic characteristics. J Surg Oncol 1988; 38:275.

32. Cozen W, Bernstein L, Wang F, et al. The risk of angiosarcoma following primary breast cancer. Br J Cancer 1999; 81:532.
33. Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology 2020; 53:3.
34. Warren AG, Brorson H, Borud LJ, Slavin SA. Lymphedema: a comprehensive review. Ann Plast Surg 2007; 59:464.
35. McDuff SGR, Mina AI, Brunelle CL, et al. Timing of Lymphedema After Treatment for Breast Cancer: When Are Patients Most At Risk? Int J Radiat Oncol Biol Phys 2019; 103:62.
36. Merchant SJ, Chen SL. Prevention and management of lymphedema after breast cancer treatment. Breast J 2015; 21:276.
37. Shaw C, Mortimer P, Judd PA. A randomized controlled trial of weight reduction as a treatment for breast cancer-related lymphedema. Cancer 2007; 110:1868.
38. Stout Gergich NL, Pfalzer LA, McGarvey C, et al. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer 2008; 112:2809.
39. Lette J. A simple and innovative device to measure arm volume at home for patients with lymphedema after breast cancer. J Clin Oncol 2006; 24:5434.
40. Ancukiewicz M, Russell TA, Otoole J, et al. Standardized method for quantification of developing lymphedema in patients treated for breast cancer. Int J Radiat Oncol Biol Phys 2011; 79:1436.
41. McLaughlin SA, Staley AC, Vicini F, et al. Considerations for Clinicians in the Diagnosis, Prevention, and Treatment of Breast Cancer-Related Lymphedema: Recommendations from a Multidisciplinary Expert ASBrS Panel : Part 1: Definitions, Assessments, Education, and Future Directions. Ann Surg Oncol 2017; 24:2818.
42. Ward LC, Dylke E, Czerniec S, et al. Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. Lymphat Res Biol 2011; 9:47.
43. Moseley A, Piller N. Reliability of bioimpedance spectroscopy and tonometry after breast conserving cancer treatment. Lymphat Res Biol 2008; 6:85.
44. Mayrovitz HN, Weingrad DN, Davey S. Local tissue water in at-risk and contralateral forearms of women with and without breast cancer treatment-related lymphedema. Lymphat Res Biol 2009; 7:153.
45. Ward LC, Czerniec S, Kilbreath SL. Operational equivalence of bioimpedance indices and perometry for the assessment of unilateral arm lymphedema. Lymphat Res Biol 2009; 7:81.

46. McLaughlin SA, DeSnyder SM, Klimberg S, et al. Considerations for Clinicians in the Diagnosis, Prevention, and Treatment of Breast Cancer-Related Lymphedema, Recommendations from an Expert Panel: Part 2: Preventive and Therapeutic Options. Ann Surg Oncol 2017; 24:2827.

47. Society for Ambulatory Anesthesia (SAMBA) Statement on Intravenous Catheter Placement, Venipuncture and Blood Pressure Measurements in the Ipsilateral Upper Extremity after Breast Cancer Surgery with and without Axillary Lymph Node Dissection https://samba.memberclicks.net/assets/docs/SAMBA_Statements/SAMBA_Statement_IV-Breast-Surg.pdf (Accessed on October 19, 2021).

48. Tsai RJ, Dennis LK, Lynch CF, et al. The risk of developing arm lymphedema among breast cancer survivors: a meta-analysis of treatment factors. Ann Surg Oncol 2009; 16:1959.

49. Herd-Smith A, Russo A, Muraca MG, et al. Prognostic factors for lymphedema after primary treatment of breast carcinoma. Cancer 2001; 92:1783.

50. 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 2015; 96:1131.

51. 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 2008; 26:5213.

52. Nos C, Kaufmann G, Clough KB, et al. Combined axillary reverse mapping (ARM) technique for breast cancer patients requiring axillary dissection. Ann Surg Oncol 2008; 15:2550.

53. Cheville AL, Das I, Srinivas S, et al. A pilot study to assess the utility of SPECT/CT-based lymph node imaging to localize lymph nodes that drain the arm in patients undergoing treatment for breast cancer. Breast Cancer Res Treat 2009; 116:531.

54. Boccardo FM, Casabona F, Friedman D, et al. Surgical prevention of arm lymphedema after breast cancer treatment. Ann Surg Oncol 2011; 18:2500.

55. Markkula SP, Leung N, Allen VB, Furniss D. Surgical interventions for the prevention or treatment of lymphoedema after breast cancer treatment. Cochrane Database Syst Rev 2019; 2:CD011433.

56. Boccardo F, Casabona F, De Cian F, et al. Lymphatic microsurgical preventing healing approach (LYMPHA) for primary surgical prevention of breast cancer-related lymphedema: over 4 years follow-up. Microsurgery 2014; 34:421.

57. Paramanandam VS, Dylke E, Clark GM, et al. Prophylactic Use of Compression Sleeves Reduces the Incidence of Arm Swelling in Women at High Risk of Breast Cancer-Related

Lymphedema: A Randomized Controlled Trial. J Clin Oncol 2022; 40:2004.

58. Hasenoehrl T, Palma S, Ramazanova D, et al. Resistance exercise and breast cancer-related lymphedema-a systematic review update and meta-analysis. Support Care Cancer 2020; 28:3593.
59. National Lymphedema Network. NLN position paper: Exercise for lymphedema patients. ht tp://www.lymphnet.org/pdfDocs/nlnexercise.pdf (Accessed on December 14, 2010).
60. Simonavice E, Kim JS, Panton L. Effects of resistance exercise in women with or at risk for breast cancer-related lymphedema. Support Care Cancer 2017; 25:9.
61. Paskett ED, Le-Rademacher J, Oliveri JM, et al. A randomized study to prevent lymphedema in women treated for breast cancer: CALGB 70305 (Alliance). Cancer 2021; 127:291.
62. Stuiver MM, ten Tusscher MR, Agasi-Idenburg CS, et al. Conservative interventions for preventing clinically detectable upper-limb lymphoedema in patients who are at risk of developing lymphoedema after breast cancer therapy. Cochrane Database Syst Rev 2015; :CD009765.
63. 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 2010; 340:b5396.
64. Devoogdt N, Christiaens MR, Geraerts I, et al. Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: randomised controlled trial. BMJ 2011; 343:d5326.
65. Liang M, Chen Q, Peng K, et al. Manual lymphatic drainage for lymphedema in patients after breast cancer surgery: A systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2020; 99:e23192.
66. Paskett ED. Breast cancer-related lymphedema: attention to a significant problem resulting from cancer diagnosis. J Clin Oncol 2008; 26:5666.
67. De Groef A, Van Kampen M, Dieltjens E, et al. Effectiveness of postoperative physical therapy for upper-limb impairments after breast cancer treatment: a systematic review. Arch Phys Med Rehabil 2015; 96:1140.
68. Zimmermann A, Wozniewski M, Szklarska A, et al. Efficacy of manual lymphatic drainage in preventing secondary lymphedema after breast cancer surgery. Lymphology 2012; 45:103.
69. Ammitzbøll G, Johansen C, Lanng C, et al. Progressive resistance training to prevent arm lymphedema in the first year after breast cancer surgery: Results of a randomized controlled trial. Cancer 2019; 125:1683.

70. Lymphedema Risk Reduction Practices http://www.lymphnet.org/pdfDocs/nlnriskreduction.pdf (Accessed on May 07, 2014).
71. Cemal Y, Pusic A, Mehrara BJ. Preventative measures for lymphedema: separating fact from fiction. J Am Coll Surg 2011; 213:543.
72. 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 2016; 34:691.
73. Huang TW, Tseng SH, Lin CC, et al. Effects of manual lymphatic drainage on breast cancer-related lymphedema: a systematic review and meta-analysis of randomized controlled trials. World J Surg Oncol 2013; 11:15.
74. Lymphedema Risk Reduction Practices http://www.lymphnet.org/pdfDocs/nlnriskreduction.pdf (Accessed on June 06, 2012).
75. Ochalek K, Gradalski T, Partsch H. Preventing Early Postoperative Arm Swelling and Lymphedema Manifestation by Compression Sleeves After Axillary Lymph Node Interventions in Breast Cancer Patients: A Randomized Controlled Trial. J Pain Symptom Manage 2017; 54:346.
76. Koelmeyer LA, Borotkanics RJ, Alcorso J, et al. Early surveillance is associated with less incidence and severity of breast cancer-related lymphedema compared with a traditional referral model of care. Cancer 2019; 125:854.
77. Svensson BJ, Dylke ES, Ward LC, et al. Screening for breast cancer-related lymphoedema: self-assessment of symptoms and signs. Support Care Cancer 2020; 28:3073.
78. Swedborg I, Norrefalk JR, Piller NB, Asard C. Lymphoedema post-mastectomy: is elevation alone an effective treatment? Scand J Rehabil Med 1993; 25:79.
79. Bloomquist K, Oturai P, Steele ML, et al. Heavy-Load Lifting: Acute Response in Breast Cancer Survivors at Risk for Lymphedema. Med Sci Sports Exerc 2018; 50:187.
80. Keilani M, Hasenoehrl T, Neubauer M, Crevenna R. Resistance exercise and secondary lymphedema in breast cancer survivors-a systematic review. Support Care Cancer 2016; 24:1907.
81. Moseley AL, Piller NB. Exercise for Limb Lymphoedema: Evidence that it is beneficial. J Lymphoedema 2008; 3:51.
82. Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med 2009; 361:664.
83. Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 2006; :CD005001.

84. McKenzie DC, Kalda AL. Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. J Clin Oncol 2003; 21:463.

85. Ahmed RL, Thomas W, Yee D, Schmitz KH. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. J Clin Oncol 2006; 24:2765.

86. Sagen A, Kåresen R, Risberg MA. Physical activity for the affected limb and arm lymphedema after breast cancer surgery. A prospective, randomized controlled trial with two years follow-up. Acta Oncol 2009; 48:1102.

87. Singh B, Disipio T, Peake J, Hayes SC. Systematic Review and Meta-Analysis of the Effects of Exercise for Those With Cancer-Related Lymphedema. Arch Phys Med Rehabil 2016; 97:302.

88. Chan DN, Lui LY, So WK. Effectiveness of exercise programmes on shoulder mobility and lymphoedema after axillary lymph node dissection for breast cancer: systematic review. J Adv Nurs 2010; 66:1902.

89. McNeely ML, Campbell K, Ospina M, et al. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Database Syst Rev 2010; :CD005211.

90. Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial. JAMA 2010; 304:2699.

91. Devoogdt N, Christiaens M-R, Geraerts I, et al. Is Manual Lymph Drainage Applied after Axil lary Lymph Node Dissection for Breast Cancer Effective To Prevent Arm Lymphoedema? A R andomised Controlled Trial. Abstract S5-3, presented at the 33rd Annual San Antonio Breast Conference, December 8-12, 2010. Available online at http://www.abstracts2view.com/sabc s10/view.php?nu=SABCS10L_434&terms= (Accessed on February 07, 2011).

92. Schmitz KH, Cheville A, Ahmed RL, Troxel A. Balancing Risks of Deconditioning vs. Weight-Li fting for Breast Cancer Survivors.Abstract ES9-3, presented at the 33rd Annual San Antonio Breast Conference, December 8-12, 2010. Available online at http://www.abstracts2view.co m/sabcs10/view.php?nu=SABCS10L_9027&terms= (Accessed on February 07, 2011).

93. Jakes AD, Twelves C. Breast cancer-related lymphoedema and venepuncture: a review and evidence-based recommendations. Breast Cancer Res Treat 2015; 154:455.

94. National Lymphedema Network. Air travel http://www.lymphnet.org/pdfDocs/nlnairtravel.p df (Accessed on October 14, 2015).

95. 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 2010; 120:649.

96. Casley-Smith JR, Casley-Smith JR. Lymphedema initiated by aircraft flights. Aviat Space Environ Med 1996; 67:52.

97. Graham PH. Compression prophylaxis may increase the potential for flight-associated lymphoedema after breast cancer treatment. Breast 2002; 11:66.

98. Casley-Smith JR. Alterations of untreated lymphedema and it's grades over time. Lymphology 1995; 28:174.

99. Shaitelman SF, Cromwell KD, Rasmussen JC, et al. Recent progress in the treatment and prevention of cancer-related lymphedema. CA Cancer J Clin 2015; 65:55.

100. Harris SR, Hugi MR, Olivotto IA, et al. Clinical practice guidelines for the care and treatment of breast cancer: 11. Lymphedema. CMAJ 2001; 164:191.

101. Position Statement of the National Lymphedema Network: The Diagnosis and Treatment of Lymphedema. http://www.lymphnet.org/pdfDocs/nlntreatment.pdf (Accessed on May 10, 2012).

102. McNeely ML, Peddle CJ, Yurick JL, et al. Conservative and dietary interventions for cancer-related lymphedema: a systematic review and meta-analysis. Cancer 2011; 117:1136.

103. Badger CM, Peacock JL, Mortimer PS. A randomized, controlled, parallel-group clinical trial comparing multilayer bandaging followed by hosiery versus hosiery alone in the treatment of patients with lymphedema of the limb. Cancer 2000; 88:2832.

104. McNeely ML, Magee DJ, Lees AW, et al. The addition of manual lymph drainage to compression therapy for breast cancer related lymphedema: a randomized controlled trial. Breast Cancer Res Treat 2004; 86:95.

105. Ezzo J, Manheimer E, McNeely ML, et al. Manual lymphatic drainage for lymphedema following breast cancer treatment. Cochrane Database Syst Rev 2015; :CD003475.

106. Szuba A, Cooke JP, Yousuf S, Rockson SG. Decongestive lymphatic therapy for patients with cancer-related or primary lymphedema. Am J Med 2000; 109:296.

107. Zanolla R, Monzeglio C, Balzarini A, Martino G. Evaluation of the results of three different methods of postmastectomy lymphedema treatment. J Surg Oncol 1984; 26:210.

108. Casley-Smith JR, Boris M, Weindorf S, Lasinski B. Treatment for lymphedema of the arm--the Casley-Smith method: a noninvasive method produces continued reduction. Cancer 1998; 83:2843.

109. Leduc O, Leduc A, Bourgeois P, Belgrado JP. The physical treatment of upper limb edema. Cancer 1998; 83:2835.

110. Williams AF, Vadgama A, Franks PJ, Mortimer PS. A randomized controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. Eur J Cancer Care (Engl) 2002; 11:254.

111. Johansson K, Albertsson M, Ingvar C, Ekdahl C. Effects of compression bandaging with or without manual lymph drainage treatment in patients with postoperative arm lymphedema. Lymphology 1999; 32:103.

112. Johansson K, Lie E, Ekdahl C, Lindfeldt J. A randomized study comparing manual lymph drainage with sequential pneumatic compression for treatment of postoperative arm lymphedema. Lymphology 1998; 31:56.

113. Andersen L, Højris I, Erlandsen M, Andersen J. Treatment of breast-cancer-related lymphedema with or without manual lymphatic drainage--a randomized study. Acta Oncol 2000; 39:399.

114. Lasinski BB, McKillip Thrift K, Squire D, et al. A systematic review of the evidence for complete decongestive therapy in the treatment of lymphedema from 2004 to 2011. PM R 2012; 4:580.

115. Ko DS, Lerner R, Klose G, Cosimi AB. Effective treatment of lymphedema of the extremities. Arch Surg 1998; 133:452.

116. Boris M, Weindorf S, Lasinkski S. Persistence of lymphedema reduction after noninvasive complex lymphedema therapy. Oncology (Williston Park) 1997; 11:99.

117. Hamner JB, Fleming MD. Lymphedema therapy reduces the volume of edema and pain in patients with breast cancer. Ann Surg Oncol 2007; 14:1904.

118. Morgan RG, Casley-Smith JR, Mason MR, Casley-Smith JR. Complex physical therapy for the lymphoedematous arm. J Hand Surg Br 1992; 17:437.

119. Casley-Smith JR, Casley-Smith JR. Modern treatment of lymphoedema. I. Complex physical therapy: the first 200 Australian limbs. Australas J Dermatol 1992; 33:61.

120. Boris M, Weindorf S, Lasinski B, Boris G. Lymphedema reduction by noninvasive complex lymphedema therapy. Oncology (Williston Park) 1994; 8:95.

121. Daane S, Poltoratszy P, Rockwell WB. Postmastectomy lymphedema management: evolution of the complex decongestive therapy technique. Ann Plast Surg 1998; 40:128.

122. Brorson H, Svensson H. Complete reduction of lymphoedema of the arm by liposuction after breast cancer. Scand J Plast Reconstr Surg Hand Surg 1997; 31:137.

123. Filippetti M, Santoro E, Graziano F, et al. Modern therapeutic approaches to postmastectomy brachial lymphedema. Microsurgery 1994; 15:604.

124. Mondry TE, Riffenburgh RH, Johnstone PA. Prospective trial of complete decongestive therapy for upper extremity lymphedema after breast cancer therapy. Cancer J 2004; 10:42.

125. Szuba A, Achalu R, Rockson SG. Decongestive lymphatic therapy for patients with breast carcinoma-associated lymphedema. A randomized, prospective study of a role for

adjunctive intermittent pneumatic compression. Cancer 2002; 95:2260.

126. Pinell XA, Kirkpatrick SH, Hawkins K, et al. Manipulative therapy of secondary lymphedema in the presence of locoregional tumors. Cancer 2008; 112:950.
127. Gradalski T, Ochalek K, Kurpiewska J. Complex Decongestive Lymphatic Therapy With or Without Vodder II Manual Lymph Drainage in More Severe Chronic Postmastectomy Upper Limb Lymphedema: A Randomized Noninferiority Prospective Study. J Pain Symptom Manage 2015; 50:750.
128. Dayes IS, Whelan TJ, Julian JA, et al. Randomized trial of decongestive lymphatic therapy for the treatment of lymphedema in women with breast cancer. J Clin Oncol 2013; 31:3758.
129. Didem K, Ufuk YS, Serdar S, Zümre A. The comparison of two different physiotherapy methods in treatment of lymphedema after breast surgery. Breast Cancer Res Treat 2005; 93:49.
130. Szolnoky G, Lakatos B, Keskeny T, et al. Intermittent pneumatic compression acts synergistically with manual lymphatic drainage in complex decongestive physiotherapy for breast cancer treatment-related lymphedema. Lymphology 2009; 42:188.
131. Dini D, Del Mastro L, Gozza A, et al. The role of pneumatic compression in the treatment of postmastectomy lymphedema. A randomized phase III study. Ann Oncol 1998; 9:187.
132. Moattari M, Jaafari B, Talei A, et al. The effect of combined decongestive therapy and pneumatic compression pump on lymphedema indicators in patients with lymphedema secondary to breast cancer treatment: a randomized clinical control trial. Breast J 2013; 19:114.
133. Haghighat S, Lotfi-Tokaldany M, Yunesian M, et al. Comparing two treatment methods for post mastectomy lymphedema: complex decongestive therapy alone and in combination with intermittent pneumatic compression. Lymphology 2010; 43:25.
134. Uzkeser H, Karatay S, Erdemci B, et al. Efficacy of manual lymphatic drainage and intermittent pneumatic compression pump use in the treatment of lymphedema after mastectomy: a randomized controlled trial. Breast Cancer 2015; 22:300.
135. Kozanoglu E, Basaran S, Paydas S, Sarpel T. Efficacy of pneumatic compression and low-level laser therapy in the treatment of postmastectomy lymphoedema: a randomized controlled trial. Clin Rehabil 2009; 23:117.
136. Pappas CJ, O'Donnell TF Jr. Long-term results of compression treatment for lymphedema. J Vasc Surg 1992; 16:555.
137. Shao Y, Qi K, Zhou QH, Zhong DS. Intermittent pneumatic compression pump for breast cancer-related lymphedema: a systematic review and meta-analysis of randomized

controlled trials. Oncol Res Treat 2014; 37:170.

138. Torrisi JS, Joseph WJ, Ghanta S, et al. Lymphaticovenous bypass decreases pathologic skin changes in upper extremity breast cancer-related lymphedema. Lymphat Res Biol 2015; 13:46.

139. Patel KM, Manrique O, Sosin M, et al. Lymphatic mapping and lymphedema surgery in the breast cancer patient. Gland Surg 2015; 4:244.

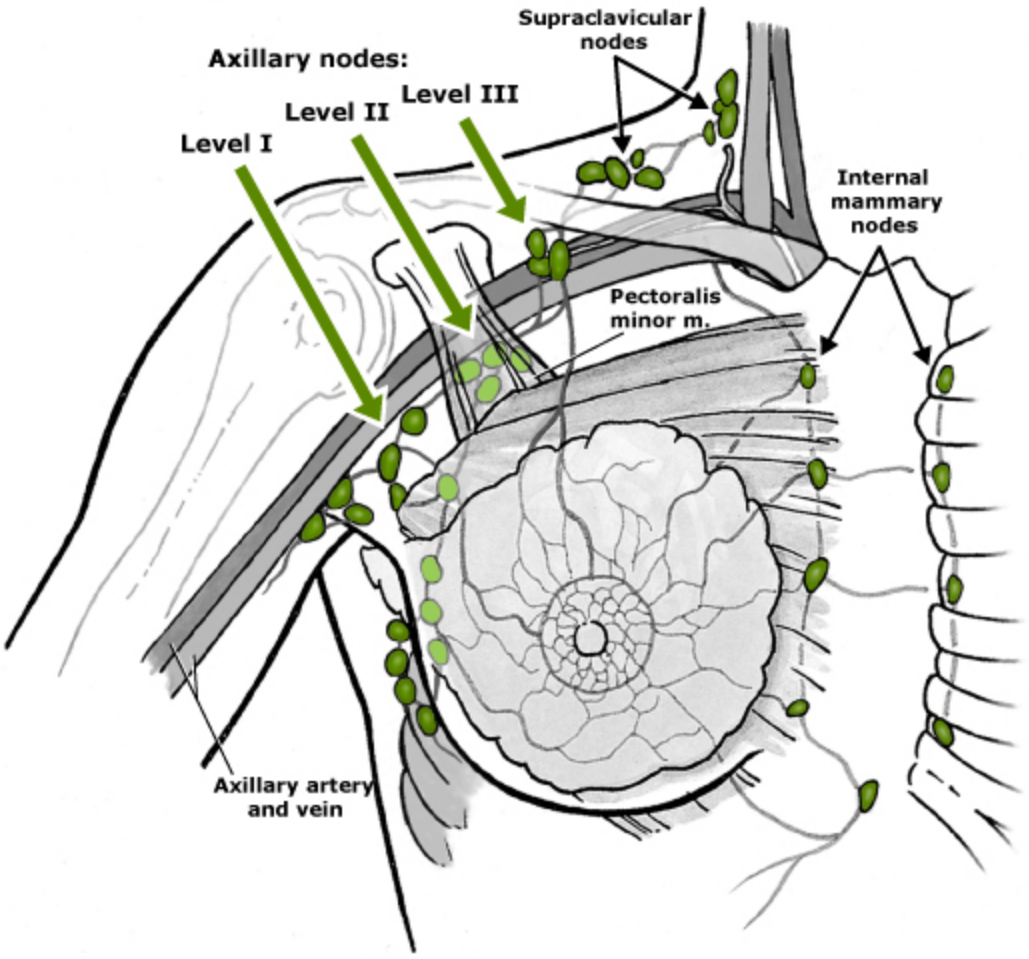
140. Brorson H, Ohlin K, Olsson G, et al. Quality of life following liposuction and conservative treatment of arm lymphedema. Lymphology 2006; 39:8.

141. Cheville AL, Andrews K, Kollasch J, et al. Adapting lymphedema treatment to the palliative setting. Am J Hosp Palliat Care 2014; 31:38.

Topic 104714 Version 34.0

GRAPHICS

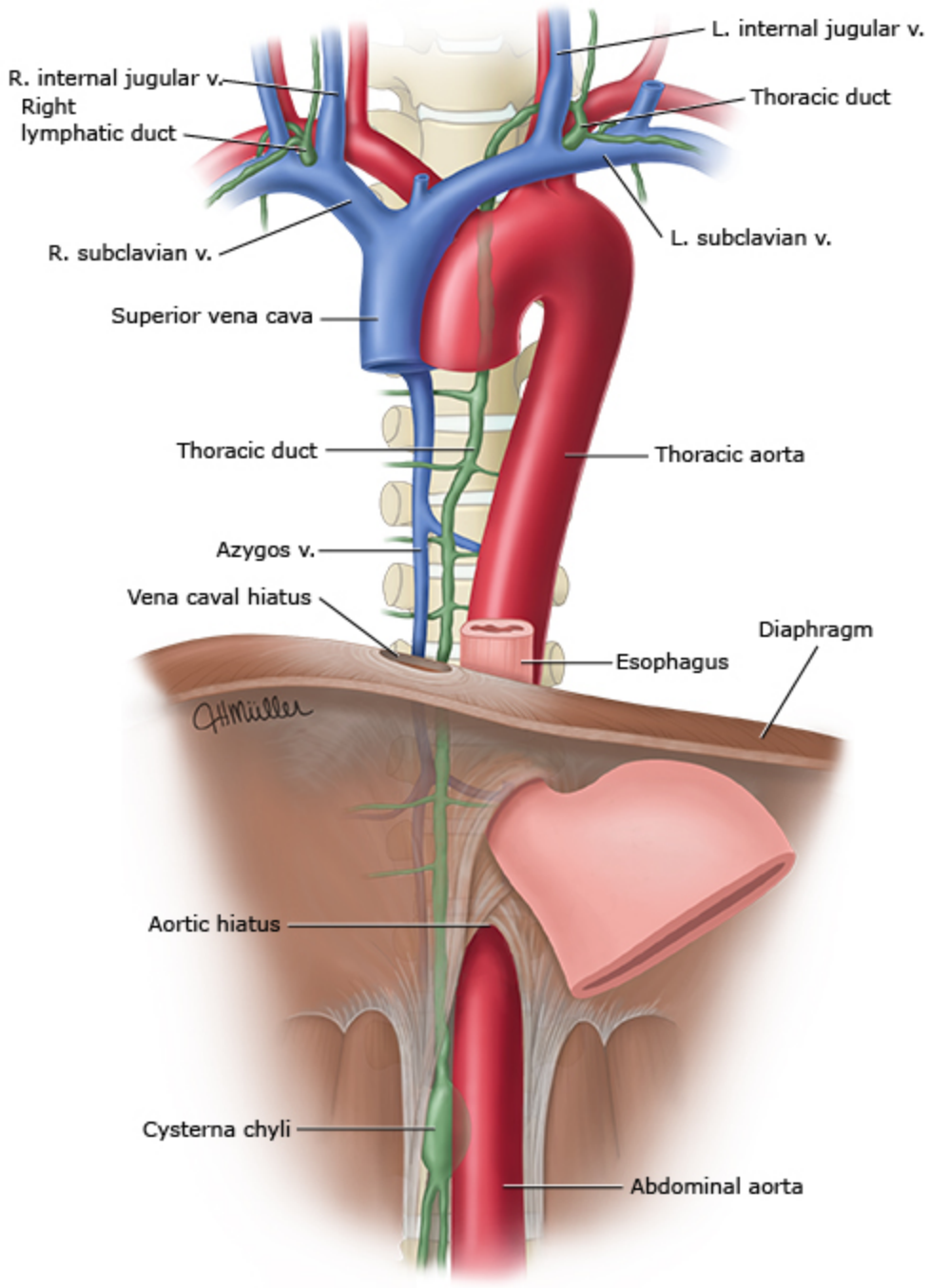
Lymphatic drainage of the breast



The lymphatic drainage of the breast flows toward the axillary and internal mammary lymph nodes.

Graphic 74746 Version 4.0

Anatomy of the thoracic duct



Course of the thoracic duct. Although wide anatomic variation exists, in most patients (40 to 60 percent), the left thoracic duct ascends from the cisterna chyli, which is a sac located just anterior to the first or second lumbar vertebra and which receives drainage from the intestinal and two lumbar lymphatic trunks. The thoracic duct passes through the aortic hiatus of the diaphragm into the posterior mediastinum continuing cephalad between the aorta and azygos vein until approximately the level of the fifth thoracic vertebra where it passes behind the esophagus. Below the fifth thoracic vertebra, the thoracic duct is commonly a dual or plexiform duct but it becomes a single 2 to 3 mm duct above that level. The

thoracic duct continues cephalad adjacent the esophagus passing posterior to the aortic arch and left subclavian artery. It then arches over the subclavian artery descending to empty either as a single (50 percent) or multiple lymphatic channels into the left subclavian vein near its confluence with the left internal jugular vein. A one-way valve at this location prevents blood from entering the thoracic duct. The right lymphatic duct drains into the right subclavian vein.

Graphic 57280 Version 9.0

Contributor Disclosures

Babak Mehrara, MD Grant/Research/Clinical Trial Support: Pfizer [Heart failure]; PureTek Corporation [Secondary lymphedema]; Regeneron Corp [Secondary lymphedema]. All of the relevant financial relationships listed have been mitigated. **Daniel F Hayes, MD** Equity Ownership/Stock Options: Inbiomotion [Breast cancer]. Patent Holder: Immunicon Corporation [Inventor]; University of Michigan [Inventor]; University of Michigan [Inventor]. Grant/Research/Clinical Trial Support: AstraZeneca [Breast cancer]; Menarini Silicon Biosystems, LLC [Breast cancer]; Pfizer [Breast cancer]. Consultant/Advisory Boards: Artiman Ventures [Breast cancer]; BioVeca [Breast cancer]; Cepheid [Breast cancer]; EPIC Sciences, Inc [Breast cancer]; Freenome, Inc [Colorectal cancer]; Guardant [Oncology]; Lexent Bio [Breast cancer]; L-Nutra [Breast cancer]; Macrogenics [Breast cancer]; OncoCyte [Biomarkers]; Predictus BioSciences [Breast cancer]; Tempus [Oncology]; Turnstone Biologics [Breast cancer]; Xilis [GI cancer]. Other Financial Interest: Menarini Silicon Biosystems [Royalties from licensing of patent – Breast cancer]. All of the relevant financial relationships listed have been mitigated. **Larissa Nekhlyudov, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose. **Eduardo Bruera, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Patricia A Ganz, MD** Consultant/Advisory Boards: Blue Note Therapeutics [Delivery of cognitive behavioral stress management to newly diagnosed breast and lung cancer patients]; Grail [Multi-cancer detection blood test]; InformedDNA [Cancer genetic testing]; Roche [Advisory board for quality of life study in clinical trial]. All of the relevant financial relationships listed have been mitigated. **Kathryn A Collins, MD, PhD, FACS** No relevant financial relationship(s) with ineligible companies to disclose. **Sadhna R Vora, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→