Management of secondary lymphedema related to breast cancer

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Abstract

OBJECTIVE To review recent literature on the management of secondary lymphedema following breast cancer.

QUALITY OF EVIDENCE MEDLINE, EMBASE, AMED, PubMed, and the Internet were searched for articles published between 2005 and 2009. Articles were evaluated using Sackett's levels of evidence. The literature search focused on primary research and systematic reviews.

MAIN MESSAGE Secondary lymphedema related to breast cancer is an ongoing challenge. Evidence suggests that there are several safe and beneficial treatments, including complex decongestive therapy, physiotherapy, and exercise. Furthermore, resistive exercises, previously contraindicated on the affected side, have been found to be both beneficial and safe with careful progression and monitoring. Exercise guidelines and patient education topics are presented with a comprehensive reference list for further reading.

CONCLUSION Advances in cancer treatment, cancer and exercise research, and lymphedema management require that physicians have a basic understanding of the current evidence to provide appropriate patient education and referral.

Résume

OBJECTIF Revoir la littérature récente sur le traitement du lymphœdème secondaire au traitement d'un cancer du sein.

QUALITÉ DES PREUVES On a consulté MEDLINE, EMBASE, AMED, PubMed ainsi que l'internet à la recherche d'articles publiés entre 2005 et 2009. Ces articles ont été évalués en utilisant les niveaux de preuve de Sackett. La recherche de la littérature portait surtout sur les recherches primaires et les revues systématiques.

PRINCIPAL MESSAGE Le lymphœdème associé au cancer du sein continue de poser un défi. Les données suggèrent qu'il existe plusieurs formes de traitement efficaces et sécuritaires, y compris un traitement décongestionnant complexe, la physiothérapie et l'exercice. En outre, on s'est rendu compte que les exercices contre résistance, autrefois contre-indiqués pour le côté atteint, sont bénéfiques et sécuritaires avec une progression et une surveillance pertinentes. L'article contient des conseils sur les exercices et les informations aux patientes, en plus d'une liste détaillée de références comme information complémentaire.

CONCLUSION Les progrès réalisés dans le traitement du cancer, la recherche sur le cancer et l'exercice, et le traitement du lymphœdème secondaire exigent que le médecin possède une connaissance de base des données actuelles s'il veut bien renseigner et diriger ses patientes.

In providing care to cancer patients and survivors, physicians might see patients presenting with secondary lymphedema, a condition in which fluid and protein accumulate in the extravascular interstitial spaces.[1-3] Lymphedema is associated with feelings of discomfort and heaviness, functional limitation, disfigurement, psychological distress, and an elevated risk of recurrent infection.[1,2,4] It has a negative effect on quality of life (QOL)[4-6] and is probably the most feared complication of breast cancer treatment.[1] Lymphedema complications can be long-lasting and are often considered to be "major."[1] Several risk factors contribute to the development or severity of secondary lymphedema (**Table 1**),[2,3,7-14] including a higher body mass index, cellulitis, and delayed onset and duration of lymphedema.[15] Background information is available in several systematic reviews.[16-26]

Lymphedema measurement

The most common methods of lymphedema measurement are bioelectrical impedance,[27] volume displacement, and circumferential measurements. Ridner et al (2007)[28] compared results from 2 types of bioimpedance instruments, infrared laser perometer, circumferential measurements, and the Lymphedema and Breast Cancer Questionnaire. They found high correlations (Pearson r 0.71 to 0.99, $P<.001$) among the tools and suggested that all could be used to assess lymphedema. Circumferential measurements were supported by Tewari et al (2008)[29] and Taylor et al (2006).[30] Volumes calculated from anatomic landmarks are reliable, valid, and more accurate than measurements based on distance from the fingers.[30] Laser scanning techniques are also valid.[31] Patients themselves play an important role in monitoring for lymphedema; however, subjective symptoms do not always correlate with measurable lymphedema.[28] Lette (2006)[32] and Lette et al (2007)[33] describe a simple, home-based volume displacement measurement kit for patients.

No effective methods are described in the literature to measure edema affecting the head, neck, breast, trunk, or genitalia. Furthermore, inconsistencies in measurement methods have led to variability in the

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Table 1. Lymphedema risk factors and incidence

ARTICLE	RISK FACTORS	INCIDENCE
Thomas-MacLean et al,[7] 2008*	>5 lymph nodes removed Postoperative infection Radiation to axilla BMI >30 kg/m^2 ≥ 2 risk factors	12%
Hayes et al,[2] 2008	Upper body symptoms at baseline Older age Being single More extensive surgery or node removal Sedentary lifestyle Treatment-related complications RT Higher BMI	8%-28%
Niwinska et al,[8] 2005	RT	10% (in breast-conserving surgery)
Clark et al,[9] 2005	Hospital skin puncture Mastectomy (vs lumpectomy or wide local incision) BMI >26 kg/m^2	20.7%
Park et al,[10] 2008	Higher staging Radical mastectomy Axillary node dissection RT BMI >25 kg/m^2	24.9%
Paskett et al,[11] 2007	Greater number of nodes removed Chemotherapy Obesity Being married	32%-54%
Ridner and Dietrich,[12] 2008	Obesity (BMI >30 kg/m^2) ≥ 3 comorbidities (eg, orthopedic issues, cardiac medications, hormone blockers, osteoporosis medications)	Not reported
Soran et al,[13] 2006	Arm infection Higher BMI Increased hand use (on affected side)	Not reported
Bani et al,[14] 2007	RT	30%
Hayes et al,[3] 2008	Older age More extensive surgery ≥1 treatment-related complication Sedentary lifestyle	33%

BMI—body mass index, RT—radiation therapy
*Canadian statistics.

reporting of lymphedema incidence and prevalence, potentially affecting clinical practice.

Incidence and prevalence

The incidence of breast cancer–related lymphedema varies greatly in the literature, ranging from 2% to 83%,[1,2,4,5,7] depending on the measurement tool used. Hayes et al (2008)[2] found that, compared with bioimpedance spectroscopy, 40% to 60% of patients measured with circumferential or self-report tools went undetected. Further, a false diagnosis of lymphedema was given to 12% of those diagnosed using circumferential tools and 40% of those using self-report instruments.[2] Other articles reported incidence rates of 33% to 48% following axillary lymph node dissection and radiation therapy (RT)[34] and 5% to 14% after sentinel node biopsy and RT.[35] In a Canadian study, the reported incidence was approximately 12%.[7] In general, the prevalence of reported lymphedema ranges from 0.6% to 54%.[1,2,11,36-39] Secondary lymphedema was more prevalent in patients who had radical mastectomy (20%) than in those who had breast-conserving surgery (8%).[39] Additionally, patients who had axillary lymph node dissection reported a higher prevalence (27%) than those who had sentinel lymph node biopsy (3%).[38]

This article provides a review of the recent literature on the management of breast cancer–related lymphedema. As front-line health care providers, family physicians have a pivotal role in educating cancer patients about the risk of lymphedema, thereby potentially helping reduce the incidence and severity of this chronic condition.

Quality of evidence

Articles were found using a comprehensive search of several electronic databases, including MEDLINE, AMED (Allied and Complementary Medicine Database), EMBASE, and PubMed, restricted to recent publications (between 2005 and 2009) with an emphasis on primary research articles in English. The search terms *lymphedema, cancer, neoplasm, exercise, physical activity, edema,* and *breast cancer* were connected using *and.* This yielded 719 articles; all abstracts were reviewed and 135 full articles were read, most of which were primary research articles and systematic reviews. The primary articles were evaluated using Sackett's levels of evidence,[40,41] ranging from 1, the strongest evidence (systematic reviews of randomized controlled trials), to 5, the weakest evidence (expert opinion without explicit critical appraisal). Further information is available from the Centre for Evidence Based Medicine (**www.cebm.net**). An Internet search for references and clinical guidelines was also conducted.

Main message

Lower incidences of lymphedema were found in women who exercised regularly, received lymphedema education before treatment, and performed preventive self-care activities.[10] Bani et al (2007)[14] found that provision of education on lymphedema was associated with use of lymph-drainage massage services. Other factors associated with lower lymphedema incidence and severity included chemotherapy and antiestrogen drugs.[15]

Two main treatments were identified in the literature for the management of breast cancer–related lymphedema: complex decongestive therapy (CDT)—also known as *combined decongestive therapy* and *complex decongestive physiotherapy*—and exercise. Complex decongestive therapy has 4 components: manual lymphatic drainage (MLD); compression therapy; remedial arm and shoulder exercises; and deep-breathing exercises to promote venous and lymphatic flow.[42] There are 2 CDT phases: the intensive first phase includes all 4 components provided by lymphedema therapists; in the second, or maintenance, phase the patient practises self-care, with periodic MLD by a therapist. Prescribed exercises aim to restore wrist, forearm, arm, shoulder, cervical, and thoracic trunk range of motion (ROM) and strength. The literature on CDT did not consistently describe the exercises prescribed or the use of MLD.

Complex decongestive therapy. Current evidence supports the use of CDT to improve QOL,[43] reduce lymphatic volume,[42,44] and increase patients' intention to exercise.[45] However the quality of the literature on CDT varied considerably (**Table 2**).[42-52] Many studies simply described CDT's effects rather than comparing treatment approaches. Didem et al (2005) were unable to demonstrate that CDT was superior to standard practice (exercise without MLD) to improve shoulder mobility.[48] In CDT's maintenance phase, patients monitor their own conditions and practise self-care[49]; reduced compliance during this phase can result in increased lymphedema.[49,50] Bernas et al (2005)[53] described massage therapy for lymphedema management.

Two studies investigated whether ongoing local disease can be influenced by CDT[47] and MLD,[46] concluding that there is no scientific evidence of increased metastasis due to either and that both are safe. Other important findings were that RT does not negatively affect the effects of CDT[51] and that the most substantial lymphedema reduction occurs within the first 3 days of intensive MLD,[52] suggesting that the intensive phase's optimal duration might be shorter than currently practised.

The literature indicates that physiotherapists play an important role in the prevention, early detection, and treatment of secondary lymphedema in cancer patients.[54-57] Treatment guidelines are available online[58] and in the literature.[59]

Exercise. Supervised exercise programs for patients with lymphedema aim to restore ROM, increase muscle strength, restore or maximize upper extremity function, and control swelling. Weight reduction alone helps lessen lymphedema.[60,61] This is important because exercise and weight reduction have been shown to help prevent breast cancer[62-65] and improve survival.[66-71] Supervised exercise can be individualized or group-based; however, to address patients' specific limitations, individualized ROM programs are advised. Although the quality of the research on the effects of exercise in women with breast cancer is higher than that evaluating CDT (**Table 3**),[72-81] the literature does not detail the exercises prescribed.

Range of motion: In the studies reviewed, postoperative rehabilitation primarily improved shoulder flexion, abduction, and external rotation. The reviewed literature lacks details of the exercises, their intensity, progression methods, or optimal group sizes. Where details were provided, exercise sessions ranged from 45 to 60 minutes, 2 to 3 times per week, for 6 to 12 weeks.

Studies have found that immediate postoperative initiation of ROM exercises improved upper extremity mobility, shoulder function, and QOL.[73,74,76] Furthermore, early intervention did not increase postoperative complications such as infections, scar development, or lymphedema.[73,74,76] A randomized controlled trial by Lauridsen

Table 2. Key findings on the role of complex decongestive therapy in lymphedema

ARTICLE	LEVEL OF EVIDENCE*	GENERAL CONCLUSION
Godette et al,[46] 2006	5	CDT cannot promote metastasis
Pinell et al,[47] 2008	5	CDT can improve lymphedema in the presence of local or regional disease
Hamner and Fleming,[44] 2007	5	CDT can reduce lymphatic volume and pain
Koul et al,[42] 2007	5	CDT and MLD with exercise are associated with substantial reduction in lymphedema
Didem et al,[48] 2005	2	CPP can improve shoulder mobility and lymphedema
Karadibak et al,[45] 2008	5	CDT can decrease edema and fear of activity, and improve QOL
Kim et al,[43] 2007	5	CDT improved QOL in maintenance phase
Johnstone et al,[49] 2006	5	Reduced compliance with CDT in maintenance phase resulted in long-term lymphedema
Vignes et al,[50] 2007	5	Noncompliance with maintenance phase resulted in increased lymphedema
Thomas et al,[51] 2007	5	Radiation therapy did not reduce the effects of CDT
Yamamoto et al,[52] 2008	5	Most edema reduction during CDT occurred during the first days, suggesting shorter treatment periods than indicated in current practice

CDT—complex decongestive therapy, MLD—manual lymphatic drainage, CPP—complex physiotherapy program, QOL—quality of life.
*Levels of evidence range from 1, the strongest evidence (systematic reviews of randomized controlled trials), to 5, the weakest evidence (expert opinion).

Table 3. Key findings on the role of exercise in lymphedema

ARTICLE	LEVEL OF EVIDENCE*	GENERAL CONCLUSION
Moseley et al,[72] 2005	3	10-minute upper extremity exercise with deep breathing reduces lymphedema
Gordon et al,[73] 2005	3	Early physiotherapy has potential for short-term functional, physical, and QOL benefits
Kilgour et al,[74] 2008	2	Home-based exercise helps improve shoulder mobility and ROM immediately following surgery
Lauridsen et al,[75] 2005	1 or 2†	Early physiotherapy treatment did not increase complications following surgery
Cinar et al, [76] 2008	2	Early supervised exercise was superior to home-based exercise; neither increased lymphedema
Johansson et al,[77] 2005	2	Low-intensity resistive exercises resulted in acute lymphedema that resolved after 24 hours; use of compression garments did not affect swelling
De Rezende et al,[78] 2006	2	Direct supervised exercise was superior to self-exercise; no effect on lymphedema
Cheema and Gaul,[79] 2006	5	Strength exercises are safe in conditioned women
Courneya et al,[80] 2007	1	Exercise improved self-esteem, physical fitness, body composition, and chemotherapy completion rates without causing lymphedema
Ahmed et al,[81] 2006	2	Resistive exercises did not increase lymphedema

QOL—quality of life, ROM—range of motion.
*Levels of evidence range from 1, the strongest evidence (systematic reviews of randomized controlled trials), to 5, the weakest evidence (expert opinion).
†This study had a large sample size, but did not calculate confidence intervals and power to ensure that the results were not false positive.

et al (2005)[75] found that patients who started exercising either 6 or 26 weeks after surgery improved ROM without increasing lymphedema. This suggests that starting exercise many weeks after surgery is beneficial; however, the authors did not compare the effects of early initiation with delayed exercise.

Kilgour et al (2008)[74] demonstrated that a home-based exercise program is beneficial in the first 2 weeks after surgery, but did not compare this with supervised exercise. Other studies[76,78] found that supervised or directed early therapy was superior to self-directed exercise in the immediate postoperative period.

Resistance and strengthening: Historically, after breast cancer surgery, patients were advised to avoid strenuous activity and exercises on the affected side to reduce the risk of lymphedema development or exacerbation. High-quality randomized controlled trials,[80,81] supported by other studies,[77,79] have demonstrated that resistive exercises neither cause nor worsen lymphedema. Johansson et al (2005)[77] found that low-intensity resistance exercises caused a temporary (24-hour) acute increase in lymphedema. Use of compression garments during exercise did not affect this acute lymphedema development.[77] The benefits of resistive exercises include reduced lymphedema[77] with improvements in self-esteem, physical fitness, body composition,[80] QOL,[79] and chemotherapy completion rates.[80]

Some studies that evaluated the effects of resistance prescribed low-intensity exercises[77] or progressed them very cautiously.[81] Alternately, Courneya et al (2007)[80] and Cheema and Gaul (2006)[79] prescribed resistive exercises based on estimated 1-repetition maximums (the maximum amount of weight a person can lift in a single repetition), and found no increases in lymphedema. Resistance exercises should address all the main upper extremity muscles.

Other forms of exercise might also be beneficial. Aqua lymphatic therapy helps with lower extremity swelling; however, research supporting its use for upper extremity lymphedema was not found.[82] Parbhoo (2006)[83] recommended the use of compression garments during swimming or pool therapy. Dance was shown to have neither beneficial nor detrimental effects on lymphedema.[84]

Other lymphedema treatments. Although exercise should be standard treatment for secondary lymphedema, other options exist. Weight reduction alone is beneficial for reducing lymphedema,[60,61] reducing the risk of cancer recurrence,[62-65] and improving survival.[66-71] Compression garments can be used as part of CDT or alone and are beneficial for subclinical lymphedema.[85] Mechanical modalities to reduce arm and breast lymphedema are also available, such as Flexitouch,[86,87] Endermologie,[88] and Deep Oscillation.[89] Invasive techniques might prove beneficial; liposuction combined with controlled compression therapy,[90] acupuncture,[91] and autologous stem cell transplant[92] are currently being investigated.

Patient education. Education about breast cancer complications, including lymphedema, increases patients' intention to exercise and has a demonstrated effect on lymphedema reduction.[93] A Canadian study[94] reported that breast cancer patients believed that they received insufficient information about secondary lymphedema.

However, providing information does not always translate to increased physical activity,[93] suggesting the importance of ongoing education and encouragement by physicians. Recommended patient education topics[93-100] outlined in **Table 4** are based on current evidence where it is available. Pretreatment education might improve breast cancer survivors' recall of information about lymphedema.[101]

Table 4. Patient education topics

TOPIC	ADVICE	COMMENTS
Air travel	Use compression garments	Evidence is scant and contradictory
Temperature	Avoid extreme heat (eg, hot tubs, sauna)	No evidence to support or negate this recommendation
Exercise and activity	Initiate exercise immediately after surgery	Exercise is an important component of successful treatment; evidence described in Table 3
Skin care	Keep skin clean, apply moisturizer daily, provide attention to nail care, and avoid trauma to skin	Goal is to prevent infections; evidence supports increased risk of infection and lymphedema with skin trauma
Limb constriction	Avoid constriction (eg, blood pressure cuffs, clothing)	Based on physiologic rationale not evidence
Obesity	Maintain a healthy BMI (< 30 kg/m^2)	Higher BMI is highly correlated with development and increased severity of lymphedema
Delayed diagnosis and treatment	Early diagnosis of lymphedema is better: early, subclinical symptoms might include subjective reporting of limb heaviness, aching, tightness, and fatigue	Early diagnosis results in more effective treatment, possible prevention, and less severe lymphedema

BMI—body mass index.

Discussion

Breast cancer–related lymphedema is an ongoing challenge for many survivors. A variety of treatments are available for the management of lymphedema, but the evidence supporting them varies. Complex decongestive therapy is a common treatment for lymphedema; however, the evidence supporting it is weaker than that supporting exercise. Based on this review we recommend the following for physicians with breast cancer patients and survivors in their care:

Patient education and referral. Physicians can play a pivotal role as educators by informing breast cancer patients about the risk of secondary lymphedema, prevention strategies, early signs and symptoms, and treatment options. Evidence shows that early intervention is the key to effective treatment. Physicians can also help their patients by referring them to trained health care providers such as physiotherapists or lymphedema therapists.

Exercise prescription and compliance. Exercise guidelines (**Table 5**) are evidence-informed targets for supervised therapy. As many patients might initially be unable to achieve these levels, exercises must be tailored to individuals' needs, abilities, and disease status. Preoperative assessment is recommended[58] to provide a baseline for postoperative rehabilitation, including exercise prescription. Physicians are encouraged to educate their breast cancer patients about the benefits of regular exercise and healthy weight for secondary lymphedema prevention and management. Ideally, physicians should refer patients to physiotherapists or exercise specialists with knowledge of cancer, its treatment, and rehabilitation.

Table 5. Exercise guidelines

TYPE	SESSION LENGTH, MIN	SESSIONS/ WK	NO. OF WK	COMMENTS
ROM	40-60	3-5	8-12	Focus on shoulder abduction, external rotation, and flexion movements Options include direct anatomic plane movements, scapular plane movements, or functional and combined movements (eg, hand behind head, which will combine all movements) There are no guidelines on the optimal number of repetitions or duration of each stretch
Strength	30-60	2	8-12	Resistive exercises should address all the main upper extremity muscle groups Use 1-RM to determine each patient's lifting weight; patients should exercise at 60%-70% of estimated 1-RM Two sets of 8-12 repetitions per exercise; increase weights when the patient can perform 12 repetitions with minimal difficulty
Endurance	45	3-5	8-12	Target heart rate should be 60%-80% of heart rate reserve (Karvonen formula) or 3-5 on the Borg Rate of Perceived Exertion

ROM—range of motion, 1-RM—1-repetition maximum.

Client-specific exercise prescription is recommended over general low-intensity exercises. The American College of Sports Medicine has published guidelines for cardiorespiratory fitness[102] and resistance training.[103] Formulas for estimating 1-repetition maximums in older adults are also available.[104] Ahmed et al (2006)[81] progressed resistance exercises cautiously, and only after measurements showed no increases in lymphedema.

The evidence supports exercise during cancer treatment; however, some patients might have difficulty exercising before their treatment ends. According to Moseley et al (2005),[72] gentle arm exercises with deep breathing were effective in reducing lymphedema and had a 90% compliance rate; however, these reductions were not as substantial as those resulting from other treatments.

Conclusion

Secondary lymphedema continues to present a challenge to breast cancer patients and survivors. Several treatment options exist for its management. Although the literature does not identify which treatment is superior, education, exercise, and lymphatic drainage massage are important components of a successful treatment program. Recent research indicates that resistive exercises do not increase incidence or severity of lymphedema, and that such exercises can help manage the side effects of cancer treatment. However, cautious progression of strengthening exercises is essential, ideally with close monitoring by a physiotherapist. Various community-based resources to assist patients who have secondary lymphedema are outlined in **Table 6**.

Further research on lymphedema management should use designs that minimize biases and identify optimal treatments. To evaluate exercise prescription for lymphedema management, comprehensive information (exercise frequency, duration, mode, intensity, and progression strategy) is required. Future research could identify the exercises with the greatest effect on lymphatic drainage and evaluate efficacy at different stages of cancer treatment. It would also be beneficial for prospective trials to investigate the contribution of exercise to secondary lymphedema prevention, reversal, and management, and the long-term effects of exercise on cancer survivors' health and well-being.

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Contributors

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Competing interests

None declared

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Table 6. Lymphedema-related links and resources

ORGANIZATION	WEBSITE	CONTENT
Breast Cancer Action (Ottawa) Lymphedema: Take Control project	**www.bcaott.ca/lymphedema/info**	Patient education and health provider resources about lymphedema prevention and management, focusing on exercise
Canadian Lymphedema Framework and International Lymphoedema Framework	**http://sites.google.com/site/canadalymph/home** and **www.lympho.org/link.php**	Canadian and international collaborations promoting lymphedema research, best practice guidelines, and clinical development
CPA and the CPA Oncology Division	**www.physiotherapy.ca** and **www.oncologydivision.ca**	Help finding a physiotherapist with experience treating people with cancer
Lymphovenous Canada	**www.lymphovenous-canada.ca**	Current research, support groups, and help finding certified therapists
Vodder School of North America	**www.vodderschool.com/find_a_therapist**	Help finding Vodder-certified lymphedema therapists

CPA—Canadian Physiotherapy Association.

EDITOR'S KEY POINTS

- Secondary lymphedema is a common medical complication following treatment of breast cancer and it requires medical attention. Physicians should be able to identify secondary lymphedema, provide basic patient education, and refer patients to other health care providers for further treatment.
- Lymphedema can be treated with patient education, complex decongestive therapy, self-massage, and exercise.
- Exercise is a beneficial and safe modality that can be used to prevent and manage secondary lymphedema.
- Postoperative rehabilitation improves shoulder flexion, abduction, and external rotation and should be offered to all breast cancer patients before commencement of strengthening exercises.
- Resistance exercises are safe but should be introduced gradually, and lymphedema development should be monitored.

POINTS DE REPÈRE DU RÉDACTEUR

- Le lymphœdème secondaire est une complication fréquente du traitement du cancer du sein; cette condition requiert une attention médicale. Le médecin devrait être capable d'identifier cette complication, de renseigner adéquatement la patiente et de la diriger vers d'autres intervenants du personnel soignant pour un traitement ultérieur.
- Le lymphœdème se traite par de l'information à la patiente, un traitement décongestionnant complexe, des massages et de l'exercice.
- L'exercice peut être utilisée de façon bénéfique et sécuritaire pour prévenir et traiter le lymphœdème.
- La réadaptation postopératoire améliore la flexion, l'abduction et la rotation externe de l'épaule; on devrait l'offrir dans tous les cas de cancer du sein avant de débuter les exercices de renforcement.
- Les exercices en résistance sont sécuritaires mais ils devraient être introduits graduellement, tout en surveillant le développement du lymphœdème.

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