ETMIS 2011; Vol. 7 : N° 3

Treatment of cancer-related Secondary Lymphedema

Summary

Prepared by

Kathy Larouche et Marie-France Witty

April 2011

Institut national d'excellence en santé et en services sociaux
Québec

SUMMARY
TREATMENT OF CANCER-RELATED SECONDARY LYMPHEDEMA

Introduction

Secondary lymphedema is a chronic disease caused by the accumulation of protein-rich lymph fluid in interstitial spaces and subcutaneous tissue, mainly adipose and connective tissue, which affects mostly the upper and lower limbs. The pathophysiological mechanism involved is the obstruction or disturbance of lymphatic flow due chiefly to surgical cancer treatment with lymph node dissection or sentinel node biopsy but also to radiation therapy or chemotherapy.

Secondary lymphedema is a relatively frequent disease. Although its incidence is not accurately known owing to the variability in the definitions and disease detection techniques, it may range from 10% to 50%, depending on the type of cancer and treatment procedure. Breast cancer is the most common form of cancer involved (approximately 80% of cases), followed by genito-urinary and gynecological cancers and melanomas.

Since the disease is likely to worsen, prevention is a key element, and a series of empirical measures to reduce its onset have been proposed. The leading measures include continuing education for healthcare providers and patients, and the adoption of preventive behaviours.

Without appropriate management, this disease may progress and the edema may worsen, causing physical discomfort, pain, functional impairment, major physical and psychological complications, long-term morbidity, and a deterioration in quality of life. Several physical, pharmacological and surgical treatment options are offered to patients with cancer-related secondary lymphedema. This disease most often requires extensive and intensive management that may be costly. Québec, however, does not have a specific lymphedema management program, and most treatments are not covered by the public health insurance plan.

In this context, the Direction de la lutte contre le cancer (DLCC)[2] asked AETMIS (now INESSS) to conduct a systematic literature review on the best management of cancer-related secondary lymphedema. This document addresses mainly the efficacy of the different therapeutic procedures. It also presents an exploratory study of the costs associated with the clinical management of secondary lymphedema.

Methodology

Various search strategies were used in MEDLINE, The Cochrane Library, EMBASE, Web of Science (1998–2010) and the INAHTA database to identify systematic reviews, health technology assessment reports, guidelines and primary studies on the efficacy of treatments for cancer-related secondary lymphedema. MEDLINE and Econlit (1999–2010) were explored to extract economics literature on the management of this disease. Studies of patients with primary lymphedema, secondary to but not caused by the treatment of cancer, and with bilateral or self-diagnosed lymphedema were excluded. Owing to the heterogeneous treatment modalities used and diverse types of outcomes identified, the evidence was not analyzed collectively and is presented separately. The randomized controlled trials were specifically analyzed by means of an evaluation checklist measuring their methodological quality and bias risks.

In this report, the main outcome measure used to assess the efficacy of the treatments was affected limb volume or circumference reduction post procedure. A loss of at least 10% or 200 mL was considered clinically significant. Quality of life and other associated factors, especially pain and mobility in the ipsilateral limb, were also considered when measured in the efficacy studies.

For the purpose of estimating the treatment costs for cancer-related secondary lymphedema in Québec, a budget impact model was developed based on the therapeutic modalities supported by some scientific evidence of efficacy. The opinions of Québec experts in the physical rehabilitation field (physiotherapists, massage therapists, orthopedic equipment suppliers, and administrators) were also sought (telephone or personal interviews) to contextualize the selected treatment modalities and to complete the information missing from the literature. A per-patient cost was estimated for the intensive and maintenance phases of the treatment. The cost of the intensive phase is usually non-recurring, whereas the cost of the maintenance phase is recurring and generally lifelong. The estimation of the total cost and necessary resources to treat all affected people is also presented for the first five years of complete lymphedema treatment coverage by the Ministère de la Santé et des Services sociaux (MSSS).

---

[2] Now the Direction québécoise du cancer

Results

Efficacy of therapeutic procedures

This report targeted all therapeutic procedures currently used for the treatment of cancer-related secondary lymphedema, including, on the one hand, physical treatments, such as complex decongestive therapy, multi-layered low-stretch bandaging, manual lymphatic drainage, pneumatic compression, low-level laser therapy, compression garments and physical exercises, and, on the other hand, oral medications and surgical procedures, especially liposuction and lymphovenous anastomosis.

Most of the studies reviewed were of poor methodological quality and were conducted on small patient samples with relatively short post-treatment follow-up periods. In the review of the literature, which contained a very large number of controlled studies and case series, only a few randomized controlled trials of medium quality presenting moderate risks of methodological bias were selected.

The best lymphedema management takes place in two distinct phases: an intensive phase, ranging from two to four weeks and designed to reduce lymphedema volume, followed by a maintenance phase, aimed at maintaining the volume reduction.

Intensive-phase treatment

Despite the limited quality of the evidence analyzed, convergence exists on the efficacy of the different physical treatments. According to the available evidence, multi-layered low-stretch compression bandages may be generally effective for reducing lymphedema in the upper limbs. Manual lymphatic drainage performed by a properly trained health professional may have a short-term effect on volume reduction when used as a treatment modality alone. However, the results are contradictory about the actual benefits produced by adding this type of massage to multi-layered low-stretch compression bandages. A few studies seem to show a mild synergistic effect on volume reduction, especially in the case of moderate lymphedema. Manual lymphatic drainage may nonetheless give patients a sense of comfort, a relaxing effect, a decrease in skin tension, and privileged contact with a care provider. As such, it may have a positive effect on the management of secondary lymphedema by improving patients' quality of life.

Regarding the surgical approach, the evidence analyzed seems to indicate that liposuction may be somewhat effective for a very specific type of secondary lymphedema, especially advanced stage II lymphedema. This type of treatment is still experimental, however, and performed only by a team in a centre in Sweden or by surgeons trained in that centre. To our knowledge, it is not offered in Québec. Moreover, it is essential for patients to wear compression garments permanently (24 hours a day) after the operation to maintain volume reductions.

The efficacy of the other types of physical and surgical treatments, such as pneumatic compression, low-level laser therapy, physical exercises, lymphovenous anastomosis and surgical resection, used alone or in combination with other treatments, has not been demonstrated. However, physical aerobic or resistance exercises do not seem to have adverse effects. There is no evidence supporting the efficacy of oral medications and supplements.

Maintenance phase

Very few studies have specifically examined the maintenance phase, and they are of poor methodological quality. However, they do converge on one point: the maintenance phase is crucial for maintaining the volume reductions achieved during the intensive-phase treatment, and non-compliance with the instructions for this phase is the primary factor contributing to the loss of the hard-won gains acquired during the intensive phase. Volume regain may lead to several complications, especially fibrosis, infections, decreased range of motion and pain.

The evidence analyzed seems to show that it is essential for patients to wear compression garments regularly. Manual lymphatic drainage may not be indispensable and may be replaced with simple lymphatic drainage (self-massage).

Treatment costs

The services currently offered in Québec's public health system are very limited. According to the preliminary budget impact analysis performed, intensive-phase treatment would cost on average $422 per patient. This cost takes into account the average cost of inelastic upper-limb compression bandages ($55), the cost of a physiotherapist's assessment ($37) and the cost of bandage application ($330) for a period of 15 treatment sessions. If the plateau of lymphedema reduction were reached in 6 sessions, the cost of treatment would be $132, whereas it would rise to $440 if the plateau were reached in 20 sessions. The average total annual cost for intensive-phase treatment in the first five years of a public lymphedema management program would be $219,700 or $329,500, depending on the selected proportion (10% or 15% respectively) of patients treated for secondary lymphedema related to breast cancer, based on an average annual increase in breast cancer incidence of 0.16%. These costs were calculated from the total average per-patient cost ($422).

Maintenance-phase treatment would annually cost $1,217 on average per patient. This cost includes the average equivalent annual cost of two sets of compression garments (gauntlet and sleeve) of $1,166 per year and of professional services of $51. In total, maintenance-phase treatment in the first five years of a lymphedema management program would range from $6 million to $9 million at the start of the program and would increase annually to reach from $8 million to $12 million by the fifth year of the program, according to the selected hypothesis on the incidence of secondary lymphedema to be treated (10% or 15% respectively).

Conclusions and recommendations

This report assessed the issue of cancer-related secondary lymphedema diagnosis and management.

Cancer-related secondary lymphedema is a chronic, incurable disease with an unpredictable and relatively frequent onset manifesting as an accumulation of lymph fluid generally in the upper or lower limbs. This is a disease that causes major physical problems, such as an increase in affected limb volume, pain, and movement limitation, combined with a high risk of skin infections and subcutaneous fibrosis. It erodes patients' quality of life and may lead to psychological problems such as anxiety and depression. Added to this are social costs, including social isolation and the inability to return to work, and the financial costs of medical supplies and care. It should nevertheless be noted that new diagnostic and therapeutic approaches, especially for breast cancer, may lower the incidence of lymphedema.

There are several physical, surgical and pharmacological treatment options aimed at halting the progression of the disease, reducing edema volume, limiting its complications and improving quality of life. Among the various treatments examined, the evidence analyzed converges on the efficacy of multi-layered low-stretch compression bandages for reducing edema volume during the intensive phase of treatment. Manual lymphatic drainage may be less effective for reducing edema volume but may have a beneficial effect by improving patients' quality of life. Wearing compression garments on a long-term basis appears essential for maintaining the volume losses achieved during the intensive phase. The approach must be personalized to patients' needs.

Cancer-related secondary lymphedema raises several issues:

1. The first is diagnosis, which may be suspected from the subjective symptoms reported by patients or established by the objective criteria of affected limb volume percentages or increases measured with various instruments. There is general agreement on an affected limb volume difference of at least 10% or 200 mL. However, the diversity of measurement instruments and the multiple classification systems used make it difficult to establish a diagnosis and therefore to develop a specific treatment strategy based on the degree of lymphedema. There is currently no consensus on the diagnostic criteria for lymphedema.
2. The second issue is the unpredictable nature of the disease, which may occur immediately or up to several decades after cancer treatment. As a result, it is difficult to establish an accurate incidence rate, but above all patients are obliged to take lifelong precautions. Moreover, no measure has proven effective for completely preventing the onset of lymphedema.
3. The third issue is early intervention upon disease onset to prevent complications. In fact, as soon as it appears, lymphedema becomes a chronic disease. Lymphedema management aims to halt the increase in affected limb volume and to minimize it in order to limit the effects of fibrosis, skin complications and movement limitations in the affected limb.
4. The fourth issue is the complexity of lymphedema management, which requires the coordination and collaboration of several health professionals.
5. The final issue is treatment cost and financing. Without appropriate treatment, patients with secondary lymphedema are twice as vulnerable to complications requiring the use of the public health system's medical and hospital resources. Unlike other health plans in Canada and elsewhere in the world, Québec's public health insurance plan does not cover treatments for secondary lymphedema, except for limited therapeutic services offered in a few hospital centres. The paucity of public system services forces patients to turn to the private sector where they must pay treatment costs themselves.

The preliminary budget impact analysis shows that lymphedema treatment costs are not negligible for patients and that some are recurring and lifelong.

In light of these considerations, AETMIS (INESSS) recommended the following:

1. All patients with or at risk for cancer-related secondary lymphedema should be properly informed.

   An initial mode of information should be established before any cancer procedure and repeated upon hospital discharge. Standardized information should be provided in educational brochures indicating the risks, signs and symptoms of lymphedema, basic hygiene and safety measures, benefits of achieving or maintaining a healthy weight, advisable exercises, and a service point responding to emergencies.

2. All health professionals involved in managing patients at risk for cancer-related secondary lymphedema should be given complete information on diagnosis, prevention and the various therapeutic options available, and they should be able to refer these patients to the appropriate resources when necessary.

   This information should be provided before, during and after the cancer-treatment phase by cancer surgeons, hemato-oncologists, radiation therapists and care teams, including pivot nurses, dietitians, social workers and psychologists. In addition, family physicians should be properly informed of the risks of lymphedema onset, basic hygiene and safety measures, and available community resources.

   This therefore involves a comprehensive continuing medical education program in which the federations of general practitioners and specialists concerned should participate in collaboration with the Collège des médecins. A similar initiative should be undertaken with the professional orders concerned and interdisciplinary cancer teams.

3. Providers of physiotherapy, massage therapy and any other applicable therapy should be duly trained in manual lymphatic drainage techniques specific to lymphedema treatment (Vodder or Leduc technique, etc.) and in techniques for applying multi-layered low-stretch compression bandages.

4. A committee of expert clinicians should be formed to establish the best lymphedema management practices for Québec and to develop a program offering a continuum of integrated follow-up care and including the designation or establishment of service points accessible in all the regions of Québec. If such a program were to be developed, consideration should be given to the possibility of including patients with primary lymphedema or with secondary lymphedema unrelated to cancer (due to other surgical procedures or to severe venous problems).

   This committee, under the responsibility of a government cancer organization, should gather multidisciplinary experts in the field to develop evidence-based consensus statements on:

   - available therapeutic options for the best cancer treatments that also decrease the risk of lymphedema;
   - standardized diagnostic criteria for lymphedema and the choice of a measurement instrument;
   - all preventive measures applicable to at-risk patients in order to prevent or delay the onset of lymphedema;
   - the best therapeutic measures to control lymphedema in Québec;
   - emerging therapeutic approaches, especially liposuction, lymph node transplantation and lymphovenous anastomosis.

5. The ministère de la Santé et des Services sociaux, acting through the Direction québécoise du cancer (formerly Direction de la lutte contre le cancer), should examine modalities for the public health insurance plan to cover the costs associated with the different treatment phases of cancer-related secondary lymphedema.