MULTIDISCIPLINARY GUIDELINES FOR EARLY DIAGNOSIS AND MANAGEMENT

Robert Damstra, Carola Kaandorp

In 1999, the Dutch Institute for Healthcare Improvement (CBO) organised a task force on lymphoedema to evaluate the current literature and to propose evidence- and expert-based recommendations suitable for the national implementation of guidelines for the treatment of lymphoedema. Representatives from national medical scientific organisations (e.g. surgery, gynaecology, radiotherapy, dermatology, and others), paramedical associations and patient support groups worked for two years to create the first national guidelines for the management of the condition.

Key words

Lymphoedema
Evidence-based medicine
Multidisciplinary guidelines

Lymphoedema is a common and disabling problem, caused by a dysfunction of the lymphatic system. For the patient it leads to loss of quality of life due to swelling, discomfort, fatigue and cosmetic deformity. To develop nationally implemented, widely-accepted guidelines on lymphoedema management, a multidisciplinary working group was formed by the Dutch Institute for Healthcare Improvement (CBO) with representatives from medical scientific societies, paramedical, nursing and patient organisations.

Robert Damstra is Chairman, Dutch working group on lymphoedema, Department of Dermatology, Plebology and Lymphology, Hospital Nij, Smellinghe, Drachten, the Netherlands and Carola Kaandorp is an advisor, Dutch working group on lymphoedema, Dutch Institute for Health Improvement CBO, Utrecht, the Netherlands

Development of the document

Objectives

The objectives of the guidelines were to provide recommendations in diagnostics, early recognition, multidisciplinary treatment and follow-up of lymphoedema to physicians, paramedics, nurses, healthcare workers and patients to facilitate best practice in the management of lymphoedema.

The evidence

A systematic review of English and German literature retrieved from Medline, Cochrane and CINAHL databases up to April 2001 was carried out. Some recent, relevant articles were added to update some aspects of the guidelines. The articles were classified according to the criteria for evidence-based medicine.

Validation

An initial draft of the guidelines was developed by the working group and discussed during a national congress on 5 April, 2002 organised by the CBO. The results of these discussions were incorporated into a revised draft which was approved by all representatives in the working group on lymphoedema.

The complete guideline (Kwaliteits-instituut voor de Gezondheidszorg CBO, 2002), and a summary have been published in Dutch (Damstra and Kaandorp, 2003).

In the opinion of the working group, the guidelines are suitable for all types of lymphoedema, although most literature concerns cancer-related lymphoedema. The following is a summary of the key points covered by the guidelines, together with supporting evidence and rationale where appropriate.

Conclusions/recommendations of the guidelines

- Lymphoedema is a symptom of congenital or acquired tissue fluid accumulation that arises as a consequence of impaired lymphatic drainage, for example, after breast cancer treatment
- Early diagnosis of a swollen limb and adequate treatment are important in order to prevent irreversible changes
- Patient history and characteristic clinical presentation are essential steps in the diagnostic process. Lymphoscintigraphy gives additional information to confirm impaired lymphatic flow or abnormal distribution of lymph fluid
- Information and recommendations on precautions, preventive measurements and self-management instructions are important for all patients with (or at risk of) lymphoedema
- Treatment of lymphoedema has to be adjusted to the individual patient and may consist of several therapeutic

options, including manual lymphatic drainage (MLD). After volume reduction has been accomplished, a well-fitted compression garment is essential in the maintenance phase. Surgical procedures for lymphoedema have limited use

- Lymphoedema is treated by many medical disciplines. Based on specific knowledge gained through diagnostic evaluation and treatment, a therapeutic programme is designed. Being a chronic condition, lymphoedema requires life-long treatment and follow-up.

Pathophysiology of lymphoedema

Lymph consists of tissue fluid and accumulated proteins collected from the interstitial space by a network of capillary lymph vessels, collectors and large lymph vessels, which ultimately drain into the venous system through the thoracic duct. Lymphoedema occurs when the dynamic equilibirum in the interstitium is disturbed and the lymph transport capacity is insufficient for the amount of lymph being produced. This discrepancy can be the result of a subnormal transport capacity, or an excess in lymph production. Discrete (transient) pitting oedema is often the first sign of an insufficient lymphatic transport capacity. At a later stage, usually due to the accumulation of interstitial macromolecules, inflammatory changes are induced in the subcutaneous tissue, leading to induration and pathological changes such as fibrosis and adipose tissue formation. A side-effect of the accumulation of proteins is an increase of interstitial oncotic pressure, which leads to more oedema (Olszewski, 2003). Therefore, the classical sign of lymphoedema as an irreversible, non-pitting oedema is just the end stage of a continuum and the sign of 'pitting', or 'non-pitting' oedema, is not evidence in itself for the existence of lymphoedema.

Primary and secondary lymphoedema

The supposed aetiology of the lymph flow abnormality has led to a classification that categorises lymphoedema as either primary or secondary. Primary lymphoedema refers to a developmental or functional disorder in the lymphatics and can present early or later on in life. In some cases, a genetic base is determined and lymphoedema can also occur as part of a syndrome. Secondary lymphoedema is more common and caused by trauma, surgery or infection; although this classification is arbitrary, because often a compensated primary lymphoedema will become manifest after events such as trauma or infection, and is then erroneously called secondary lymphoedema. Scharz (1990) showed that in a group of 1000 young adults, up to 8% of the women had clinical signs of lymphoedema of the lower extremities.

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Phlebolymphoedema

Phlebolymphoedema is considered a sub-form of lymphoedema. Initially, lymph transport capacity is normal, but is overloaded by accumulation of interstitial fluid as a result of venous insufficiency (dynamic insufficiency). As a secondary effect, the lymphatic system will become defective and an accumulation of macromolecules will then contribute to further tissue oedema.

Incidence

The incidence of lymphoedema, as reported in many studies, mostly concerns breast cancer-related lymphoedema. Extended searches of literature show an incidence varying from 13–43%. Recent studies even show an increased incidence of lymphoedema up to 69% after performing a sentinel node biopsy procedure in breast cancer treatment (Mansel et al, 2006; Wilke et al, 2006). A study in 2003 showed that lymphoedema is an underestimated problem (Moffatt et al, 2003). Unfortunately, there is no standardisation of measurement methods and assessment techniques, nor are there any generally accepted criteria to define lymphoedema. Also, there is a large variation in cancer therapy protocols. Recent studies in patients with breast cancer who had just undergone a sentinel node biopsy, showed that 3–6.9% of them developed lymphoedema (Sener et al, 2001; Mansel et al, 2006; Wilke et al, 2006). The prevalence of lymphoedema after gynaecological and urological interventions in the pelvic region for cervical, vulvar, penis and bladder carcinoma varied between 20% and 60%, especially when a lymphadenectomy was performed (Gaarenstroom et al, 2003).

Diagnostics in lymphoedema

In every patient with swelling of an extremity, the face or the external genitals, the diagnosis of lymphoedema should be considered. History and physical examination are the cornerstone of the diagnosis. In early stage lymphoedema, there is just a reversible, pitting oedema. Later on, the characteristic features of accumulation of macromolecules, fibrosis and interstitial inflammation will occur. Additional diagnostics can be performed by means of a dynamic lymphoscintigraphy, which involves a subcutaneous injection of a solution of radio-labelled nanocolloid, with subsequent external scintillation detection in the regions of interest by measuring the uptake.

This method is an assessment of the functional capacity of the lymphatic system. Lymphoscintigraphy is indicated when previous investigations have failed to establish the aetiology of the swelling. For a proper interpretation of a lymph scintigram, we advise the use of standardised scintigraphy protocols to minimise inter-observer variability.

Indications for additional scintigraphy

Indications for additional scintigraphy include:

- Inexplicable oedema at a young age (<35 years)
- Oedema and swelling of unknown cause and doubts concerning lymphoedema
- Oedema during the follow-up of

patients belonging to a high-risk group in which lymph nodes were damaged or removed
- Progressive development of oedema with venous and/or neurological symptoms following oncological treatment of the regional lymph node station; it is important, in this regard, to distinguish lymphoedema as a result of (recurrent) malignancy from benign oedema
- Unilateral persistent oedema following an episode of erysipelas/cellulitis
- Lymphoedema not responding to an objective, optimally-performed treatment programme
- Discrepancy between a trauma and the (persistent) resulting swelling, for example, following an insect bite, a sprained ankle or knee surgery
- Discrepancy between the subjective symptoms of a patient and the objective measurement of the extremity's swelling.

(Early) diagnostics and effect of treatment

In patients at risk, lymphoedema assessment can be performed by taking the specific history, and measuring the volume or circumference of the affected extremity.

The following aspects should be referred to during the *specific history*:
- The manner and time of development and the course
- The effect of gravity on the oedema
- The effects of exercise, ambient temperature and pregnancy (if applicable)
- The type and nature of the symptoms
- The family history according to swelling
- The prior history and comorbidity, e.g. cellulitis
- Limitations of function
- Previous therapy.

The following aspects should be evaluated during the *specific physical examination*:
- The presence of scars from previous surgery or radiotherapy
- Signs of venous insufficiency
- The nature of the swelling: 'pitting' versus 'non-pitting', unilateral versus bilateral, proximal versus distal
- Any accompanying symptoms, such as redness, warmth, pain on palpation, hyperpigmentation, thickening of the skin with congestive papillomatosis, cutaneous hyperplasia
- Stemmer's test; when the result is positive, it is no longer possible to make a crease by pinching the skin on top of the foot at the level of the proximal phalanx of the second and third toes, as a result of thickening of the skin (fibrosis)
- Abnormalities in the nails, such as abnormal or slower growth
- Indications of recurrent tumour growth.

The results of a retrospective study support the necessity to start lymphoedema treatment early with small volume changes to improve the outcome (Ramos et al, 1999). In this study, irreversible changes such as fibrosis were shown to be less pronounced with early treatment than with delayed intervention.

All members of the CBO working group agree on the necessity of having an objective, validated volumetry method, which can be applied in a clinical or outpatient setting (Stanton et al, 2000) to follow up and to measure effectiveness of treatment.

The CBO guideline supports a strategy to improve awareness of the development of early stage lymphoedema in patients at risk, such as breast cancer-treated patients, after treatment for gynaecological, urological oncology and patients with primary lymphoedema (*Figure 1*).

Lymphoedema assessment

Unfortunately, many methods of volumetry are used for lymphoedema assessment, such as circumference measurement and water displacement volumetry. All members of the CBO working group agree on the necessity of having an objective, validated volumetry method, which can be applied in a clinical or outpatient setting (Stanton et al, 2000) to follow up and to measure effectiveness of treatment. In the literature (Stranden, 1981; Ramos et al, 1999; Stanton et al, 1997; 2000; Megens et al, 2001), absolute circumference measurement is often cited as a reliable technique. The multidisciplinary working group consider this method inadequate because the increase in circumference caused by oedema must be related to the absolute circumference. A relative method, which correlates the enlargement to the total diameter is preferable. The CBO recommend the use of the 4-point circumference measurement (Herpertz method; Herpertz, 1994) with a calculated volume percentage. This method is suitable for unilateral (risk of) oedema. Another assessment is the Kuhnke method ('4cm method'; Megens et al, 2001). An optoelectrical device might be reliable, but this has still not been validated. Neither of these methods is able to measure hand and foot volume (Stanton et al, 1997).

Currently, the water displacement method is considered to be the gold standard (Kettle et al, 1958). It can be used to measure an entire extremity (Stranden, 1981), although it is time-consuming and not suitable for daily practice. Recently, a new device has been developed to perform an inverse water volumetry method for arms, which has none of the disadvantages of classic volumetry (Damstra et al, 2006). In comparison to the classic water displacement method, it measures the deficit of water in the device, not the surplus, after placing the arm in position.

A relative volumetric change of 10% in arm volume compared to the initial (pre-operative) volume is defined as lymphoedema and needs further treatment. In other structures, smaller differences do not exclude lymphoedema (e.g. the chest wall, face or the fingers; Stanton et al, 1996). Armer et al (2005) compared four diagnostic criteria for lymphoedema and

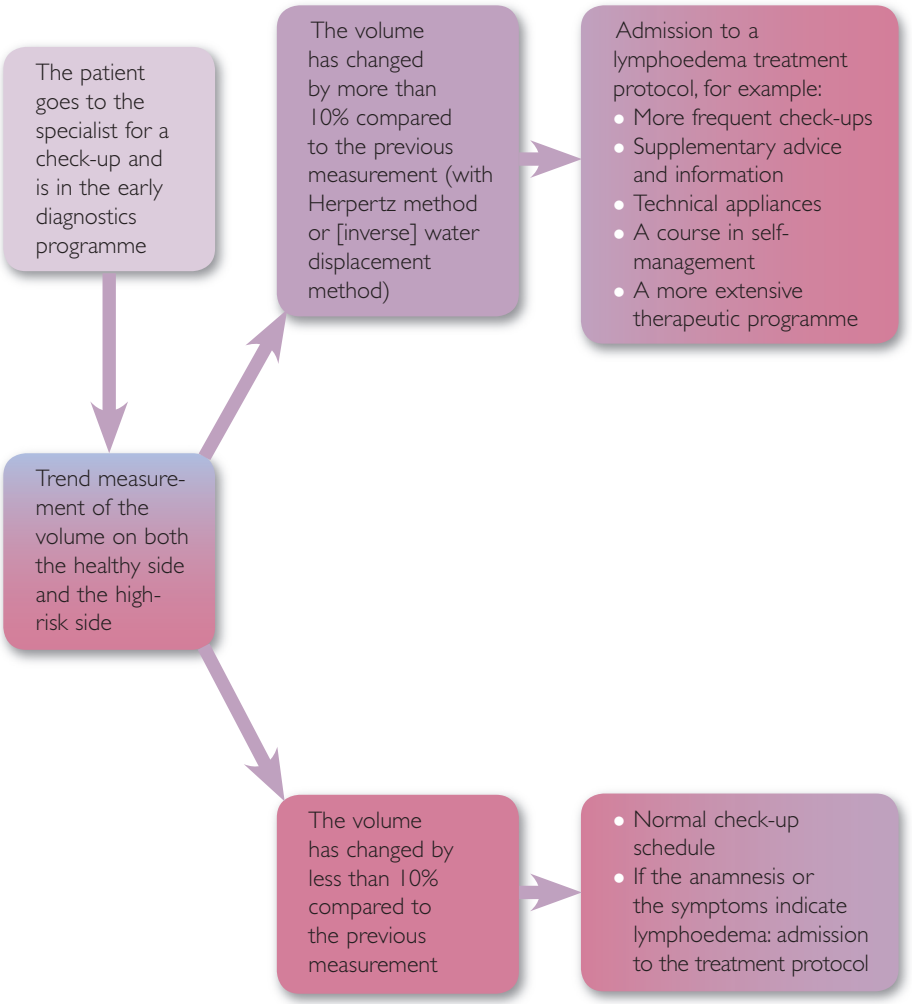

Figure 1. A scheme for early detection of lymphoedema in the extremities in at-risk patients.

also concluded that a relative volume change of 10% is very useful and corresponds to a more conservative definition of lymphoedema. This method can be performed with a validated measurement technique.

Prevention, treatment and guidance

Information and awareness

Lymphoedema interferes strongly with the quality of life and psychosocial functioning of a patient (Tobin et al, 1993; Woods et al, 1995; Logan et al, 1996; Passik and McDonald, 1998). Although no evidence-based advice is available, many precautions in preventing lymphoedema are suggested and generally accepted (National Lymphedema Network [NLN], 1998; Coward, 1999; Petrek et al, 2000). Apart from healthcare professionals working in the field of lymphoedema, there are some patient organisations active in organising support groups, courses for self-management and information on awareness of lymphoedema, e.g. the National Lymphoedema Network (NLN) in the US, the Dutch Lymphoedema Network (NLNet) in the Netherlands and the Lymphoedema Support Network (LSN) in the UK.

Early diagnostics and follow-up

In most patients, lymphoedema will develop after a period of slight, pre-clinical swelling, and is triggered by trauma, infection or over-exercise. Therefore, the consensus guideline advise programmes for early detection of swelling in patients at risk, e.g. patients treated for breast cancer or gynaecological tumours. These include routine measurement of the affected extremity, careful history-taking and physical assessment, all of which are crucial for the early detection of a decompensating lymphatic system.

For these patients, special attention will focus on the reduction of lymph production by controlling the exercise programme, wearing a preventive compression stocking on the at-risk limb, and improving lymph flow by a special training programme and a self-management course on the other limb. Also, patients are informed about special bra holders (these have broad straps which do not dig into the skin), prostheses, precautions that can be taken (e.g. skin care), and other recommendations that might apply.

Therapy of lymphoedema

Treatment should be individualised as there are many treatment options for lymphoedema that address different aspects of the disorder. Every lymphoedema therapy is concluded with the prescription of a therapeutic elastic stocking which should be worn for life.

Non-surgical treatment

In general practice, healthcare professionals are often not aware of the available therapeutic options for lymphoedema. After a proper investigation of the cause of the lymphoedema and, in the case of lymphoedema following cancer treatment, exclusion of recurrent malignancy, a conservative treatment programme should be conducted.

The goals for treatment are to eliminate oedema by stimulating lymph drainage with MLD, and reducing interstitial fluid production by compression. MLD is a specific therapeutic approach consisting of several methods of massage (Földi and Stroszenreuther, 1994). This treatment is combined with inelastic multilayer bandaging, which should be applied after each MLD session. When maximum oedema reduction is judged to have been achieved, a tailor-made compression garment should be applied to control the oedema. Other therapeutic measures include improving the function of the joints and muscle system by specific exercise and breathing techniques. Additionally, intermittent pneumatic compression (IPC) can be useful with low pressures

(<40mmHg), in combination with a MLD session in circumstances where there is no proximal swelling to shoulder or groin/genital region.

In phlebolymphoedema, there is no indication for MLD because the lymph transport capacity is normal. The first goal of therapy is to reduce the fluid production that results from the increased intravenous pressure due to the chronic venous insufficiency. Therefore, compression by bandaging is essential.

Every successful lymphoedema treatment protocol is concluded by the application of adequate compression hosiery. Therapeutic elastic stockings must be prescribed by specialists in the field. Flat-knit stockings with a high degree of stiffness (coefficient of elasticity) and little longitudinal stretch are preferred. For lymphoedema of the legs, a compression stocking (36–46.5mmHg, or sometimes 47mmHg or higher) is preferred; while for lymphoedema of the arms, the flat-knit garments must be tailor-made. Such stockings should be replaced three times a year and worn lifelong (Swedborg, 1984).

There is currently no convincing evidence for the effectiveness of any pharmaceutical intervention in the treatment of lymphoedema. Studies have been performed for diuretics, benzopyrones and some derivatives, but no significant effect could be demonstrated in any of them (Mortimer et al, 1995; Casley-Smith, 1997; Burgois et al, 1999; Loprinzi et al, 1999).

Surgical treatment of lymphoedema

Surgical treatment of lymphoedema has a long history, mostly without any (long-term) clinical success. The surgical approaches can be categorised as reconstructive and reductive surgery. Reconstructive surgery presumes to restore the lymphatic flow. However, particularly in primary lymphoedema, there is mostly a functional insufficiency rather than an anatomical one. The CBO group was of the opinion that there may be an exceptional indication for lympho-venous shunt in patients for whom conservative treatment was not successful, and who have a total blockage, as determined by qualitative lymphoscintigraphy. These patients should only be treated by a multidisciplinary team in a lymphoedema clinic. For arm lymphoedema, reduction surgery is successful by liposuction. This has been reported to achieve a long-term effect, although patients must wear compressive arm stockings for life after the surgery (Brorson et al, 1998). For extensive elephantiasis, surgical excision procedures can be beneficial in combination with conservative treatment.

Treatment protocols can be individually designed and applied by certified therapists. Most strategies for the management of lymphoedema are based on breast cancer-related lymphoedema and give no generally accepted therapeutical or logistic guideline to cope with the problem/risk of lymphoedema (Cohen et al, 2001).

Follow-up

Every treatment of lymphoedema must be followed by objective effect measurement. The CBO working group on lymphoedema developed a protocol for systematic early detection of lymphoedema in patients at risk, and for follow-up after treatment is started.

Organisation of lymphological care

Lymphoedema is a chronic, debilitating disease that is frequently misdiagnosed, treated too late, or not treated at all (Szuba et al, 2003). The medical profession should increase its efforts to diagnose lymphoedema earlier. Treatment protocols can be individually designed and applied by certified therapists. Most strategies for the management of lymphoedema are based on breast cancer-related lymphoedema and give no generally accepted therapeutical or logistical guidelines to cope with the problem/risk of lymphoedema (Cohen et al, 2001). For good management, a widely-accepted guideline is needed that can form the basis for more uniform, effective and efficient care for all patients with primary or secondary lymphoedema. Lymphoedema assessment should be incorporated into the routine follow-up for all these patients.

The CBO guidelines recommend that when a volume change of more than 10% compared to the (previous) pre-operative measurement (using the Herpertz method or [inverse] water displacement method) is detected, a specific protocol should be initiated, including:

- Frequent check-ups
- Supplementary advice and information
- Technical appliances, such as bra holders, prostheses, ortheses, (semi-) orthopaedic shoes
- A course in self-management (Cohen et al, 2001; Armer and Heckathom, 2005)
- Starting or intensifying a therapeutic lymphoedema treatment programme.

The routing for a diagnostic programme and the special tasks for each of the professionals involved are shown in *Figure 2*.

Conclusion

Lymphoedema is an increasing health problem. After surviving cancer with modern anti-cancer therapy it is dispiriting that a complication such as lymphoedema is so badly recognised and, therefore, left untreated. For patients with primary lymphoedema, the situation is even worse. Quality of life depends on the morbidity and resulting irreversible changes that are a consequence of lymphoedema. It is essential that early and long-lasting treatment and follow-up are available for all patients. Intensive cooperation between all healthcare professionals is necessary to improve awareness, and to bring about the optimum

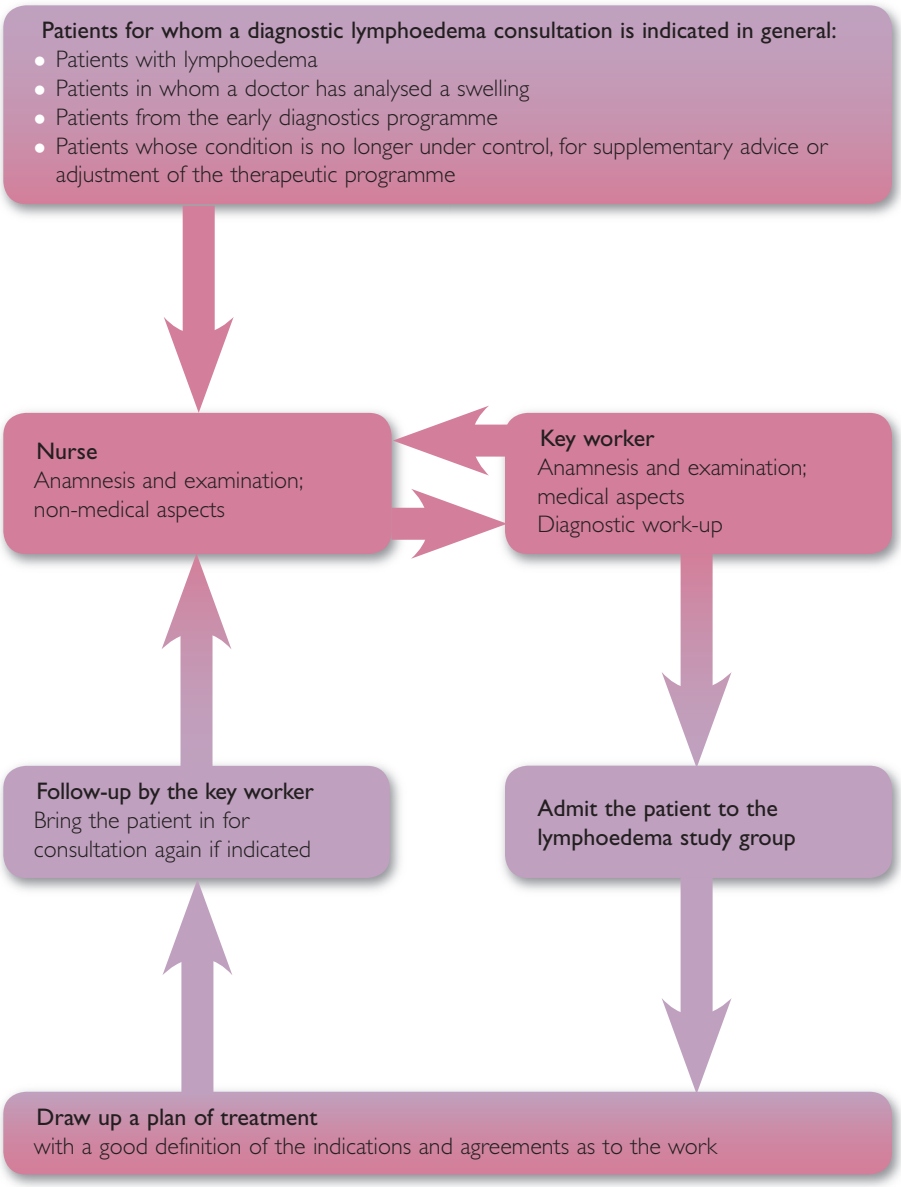

Figure 2. Recommended screening for patients with (suspected) lymphoedema.

treatment and education of these patients. This first national guidelines on lymphoedema has been accepted by consensus in the Netherlands and offers strategies and management protocols which will be beneficial for all patients suffering from the various types of lymphoedema. JL

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Key Points

- Lymphoedema is a common and disabling problem, caused by a dysfunction of the lymphatic system.
- A multidisciplinary working group was formed by the Dutch Institute for Healthcare Improvement (CBO) to achieve a national, widely-accepted guideline on lymphoedema.
- The goals for treatment are to eliminate oedema by stimulating lymph drainage with manual lymphatic drainage (MLD), and reduce interstitial fluid production by compression.
- Lymphoedema interferes strongly with the quality of life and psychosocial functioning of a patient (Tobin et al, 1993; Woods et al, 1995; Logan et al, 1996; Passik and McDonald, 1998).
- For good management, a widely-accepted guideline is needed that can form the basis for more uniform, effective and efficient care for all patients with primary or secondary lymphoedema.

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Publication of abstracts from the British Lymphology Society annual conference in the *Journal of Lymphoedema*

In the last few years the British Lymphology Society (BLS) has been keen to encourage its members to present work at its annual conference, either in the form of a poster or an oral presentation. A Research Advisory Board (RAB) has recently been formed, one of whose functions is to review the abstracts submitted for presentation at the annual conference.

For further information about the opportunity to submit abstracts for the BLS conference, which will be considered for subsequent publication in the *Journal of Lymphoedema* please go online to:

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