EFFECTIVENESS AND SAFETY OF MICROSURGERY IN LIMB LYMPHEDEMA

Spanish full text

Introduction: Lymphoedema is caused by an abnormal increase in protein-rich interstitial fluid as a result of a lymphatic circulation disorder. This accumulation causes an increase in the circumference of the affected limb, restricting its mobility and reducing patient's quality of life. The reference treatment consists of conservative measures, based on complex decongestive physiotherapy of the affected limbs, which consists of a combined program, which includes different approaches, like manual lymphatic drainage, compression therapy, physical exercise, strict skin care and patient education on hygiene- and dietary measures. These therapies slows down the progression of lymphoedema and reduce the volume of the affected limbs in the initial stages, but are not curative.

During the past years, there have been significant advances in the surgical techniques, and microsurgery is being considered as a possible alternative to conventional approaches. This assessment report was carried out at the request of the National Health System Interterritorial Council's Services, Insurance & Finance Committee, in response to a proposal from the Andalusian Regional Health Authority, to support decision making regarding their inclusion in the National Health System service portfolio. Microsurgery of lymphoedema is not available in all of Spain's Autonomous Regions (Comunidades Autónomas).

Objective: The main aims are: 1) to analyse the safety, effectiveness and efficacy of microsurgical reconstructive techniques in secondary lymphoedema among patients who do not respond to conservative treatment; and, 2) to assess the effectiveness of microsurgery of lymphoedema versus conservative treatment. The secondary aim was to analyse the organisational aspects and costs of microsurgery of lymphoedema.

Methods: To achieve the above goals, we conducted a systematic review of the literature. A specific search strategy was designed for each of the following sources of information: we reviewed leading biomedical databases, i.e., Centre for Reviews and Dissemination (CRD), Cochrane Library, Medline (Pubmed), Embase (OVID), ISI Web of Science and Scopus (SciVerse), and the databases of ongoing clinical trials (WHO International Clinical Trials Registry Platform and the US National Institutes of Health), using descriptors (MesH, Thesaurus, etc.) and adding free-text terms to address possible flaws in the indexing of some papers. The process was completed by a search using meta-search engines such as Google Scholar and the web pages of organisations and national assessment agencies. Papers were selected in accordance with a series of pre-defined selection criteria and then summarised in evidence tables. We only included prospective studies published from the year 2000 onwards.

Results: The following studies were included: 11 studies that assessed microsurgery of lymphoedema via lymphatic venous anastomosis (LVA); and 9 studies that assessed microsurgery of lymphoedema via autologous lymph node transfer (ALNT). The majority of the studies were case series covering small-sized samples, mostly of women with lymphoedema secondary to surgical treatment of breast cancer, gynaecological treatment, and/or radiotherapy. The search retrieved one randomised clinical trial which compared the results of ALNT in such patients to those of CDT. There were also two controlled non-randomised studies that assessed women with lower extremity (LE) lymphoedema; one of these studies compared the two approaches.

Of the 11 studies on LVA, only five (63%) mentioned whether there had been surgery-related adverse effects; none described severe complications and all reported favourable results. Excess

volume or volume differential in the upper extremities decreased in over half of the patients (a 22.8%-42% decrease in volume). The four studies that included LE lymphoedema, reported reductions of 4%-7%. The comparative study observed a greater reduction in volume with ALNT than with LVA (9.2% versus 7.2%). The study with the longest follow-up showed that, of 10 patients, 40% maintained a reduction in volume at 8 years but required ablative surgery, with liposuction and excision of skin and subcutaneous tissue, 20% maintained their lymphoedema stable with compression garments, and 30% died as a consequence of tumour progression.

One of the ALNT studies, which focused on undesired effects, reported that 35.7% of patients intervened in the upper extremities and 41.6% of patients intervened in the lower extremities presented with some complication. Chronic pain was the most usual problem in this study, followed by donor site lymphoedema, which affected 14.3% of patients. Other frequently described complications were infection at the lymphoid tissue harvest site (7.6%-18%), lymphorrhea (3.4%-22%), and necrosis of the graft (3.4%-18%). The improvements in volume and circumference differential in patients intervened in the upper extremities ranged from 39%-52% and 17%-50%,55% respectively vis-à-vis the value prior to surgery. The improvement in LE volume ranged from -0.03% to 39%. The sole clinical trial included showed a significant improvement in the volume and symptoms of lymphoedema in intervened patients versus the control group. Volume decreased, at one year, by a mean of 57% after surgery followed by 6 months of CDT versus 18% in patients who only received 6 months of CDT. The studies that measured quality of life using the validated Lymphoedema Quality-of-Life Questionnaire reported an improvement in global scores of 2.6 to 4.1 points, including significant improvements in the appearance, function and clinical symptom domains.

Discussion: The evidence retrieved was of low methodological quality and the studies, including the randomised clinical trial, displayed important biases (level of evidence, 2b). Although the great majority of studies reported symptomatic improvements after microsurgery, these improvements were not always assessed with objective measures, and the benefits with respect to conservative treatment are not clear. Duration of postoperative compression therapy varied widely between studies and, in one study, even within individual patients; and the same applied to the recommendation to use compression garments or other hygiene-based measures, generating important doubts as regards to how such measures might influence the final outcomes. Similarly, patients were very heterogeneous and the inclusion/ exclusion criteria were not adequately described. While reference was commonly made to the inclusion of patients who worsened or were refractory to conservative treatment, the majority of studies furnished no information on previous treatments or how lack of response had been rated. A further limitation resided in the fact that there was a lack of evidence as to the effect of microsurgery with LVA on long-term improvement of lymphoedema. Most of the studies assessed had follow-up periods of less than 1 year, and all studies that had follow-up periods of more than one year reported varying percentages of losses to follow-up which were not analysed in the final results.

Conclusions: 1) Currently there are no studies of sufficient quality which would allow for definitive conclusions to be drawn as regards the effectiveness and safety of microsurgery for the treatment of lymphoedema. The studies included -case series for the most part- displayed small sample sizes, losses to follow-up, lack of information on relevant variables, lack of standardisation of measures, and other important biases. 2) The great majority of studies described symptomatic improvements after microsurgery, but these improvements were not always tested with objective measures, and the benefits with respect to conservative treatment were not clear. The little information that there is indicates that these techniques are not curative and that patients continue to need physiotherapy and/or other conservative treatments. 3) The data are consistent with the

hypothesis that ALNT may achieve better results than LVA, and that such results, in turn, could be better in the upper than in the lower extremities, though there is great variability at the level of the individual studies. 4) According to the little evidence found, the safety results were worse for ALNT than for LVA, with a higher incidence of adverse effects due to all causes; some of these adverse effects, such as donor site lymphoedema and chronic pain, were severe and permanent. 5) There was a lack of evidence on the long-term effects of surgery, and existing studies report contradictory data. 6) The studies described many technical variants of the two approaches, some with a steep learning curve, without there currently being evidence to support the preferential use of one over the other. There are also important doubts about the indication of the procedure, or the association with other procedures, and it is not clear whether microsurgery is a good approach for all patients. 7) The technological requirements for performing the two microsurgical techniques are within the reach of most of Spain's existing tertiary hospitals, though their application would entail an increased workload, particularly in the Plastic and Reconstructive Surgery Departments, since the incidence of the most frequent lymphoedema, i.e., that of the upper extremities in breast cancer, ranges from 6%-30%. In terms of the skills base, it may call for professional training, though tertiary hospitals are usually equipped with professionals trained in microsurgery techniques.