

Clinical-Therapeutic Importance of Bioimpedance in Patients with Lymphedema: A Systematic Review

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ABSTRACT

Introduction: Lymphedema is characterized by abnormal accumulation of macromolecules and soft tissue fluids. Bioimpedance is a method that measures intra- and extracellular volumes by body segment, and has been currently used in lymphedema.

Objective: The objective of this study was to conduct a systematic review of the clinical-therapeutic importance of bioimpedance in patients with lymphedema.

Methodology: The present work consisted of a literature review. The systematic review made it possible to know and transcribe important subjects on clinical and therapeutic bioimpedance in patients with lymphedema. The work was carried out from September 2018 to April 2019, following the rules of systematic review - PRISMA.

Results: It was found that the variation of the interstitial fluid can be measured by bioimpedance, before and after intensive treatment of lymphedema. Bioimpedance is a noninvasive method used to evaluate interstitial fluids, including indications for lymphedema.

Conclusion: Bioimpedance is a suggested method to evaluate clinical and therapeutic follow-up in patients with lymphedema.

Keywords: Lymphedema; Lymphatic System; Diagnosis; Treatment; Bioimpedance

INTRODUCTION

Lymphedema is a clinical condition that leads to the accumulation of fluid and macromolecules in the interstitial space in soft tissues [1,2]. This accumulation results in the failure of lymphatic drainage, due to the malfunction of the valves of the lymphatic vessels [3], in this way, there is difficulty in the drainage of the liquid, causing the retention and consequently the edema, which can affect any part of the body, but it is more common at the extremities [4,5].

When not treated at the beginning, lymphedema can reach difficult-to-reverse proportions, progressing lymphedema to a more serious disease, which may even limit the patient's life [6],

which highlights the importance of early treatment of lymphedema. For treatment, a combination of therapeutic methods is recommended because there is no consensus on a single therapeutic method [7-10].

For measurement of lymphedema fluids, traditional methods are used, which include circumferential measurements of volume and by calculation, perimetry or Archimedes' Principle. But, each method measures the total volume of limb flow and is not sensitive to changes in the extra and intracellular fluid. However, there is a method that is sensitive to these changes, known as bioimpedance. This method can measure changes in the extracellular and intracellular volume of lymphedema [11,12]. In

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addition to measuring interstitial fluid, it provides the patient with a quick, easy and safe evaluation result [13,14].

Therefore, a study was carried out to review the literature on the clinical-therapeutic importance of bioimpedance in patients with lymphedema.

METHODS

The present work consisted of a literature review. The systematic review made it possible to know and transcribe important subjects on clinical and therapeutic bioimpedance in patients with lymphedema. The work was carried out from September 2018 to April 2019.

Study Design

A total of 45 clinical trials that were submitted to the eligibility analysis were checked, and after that, 26 studies were selected, following the rules of systematic review - PRISMA (Transparent reporting of systematic reviews and meta-analyses - <http://www.prisma-statement.org/>).

Search Strategy and Information Sources

The search strategy was performed in PubMed, Embase, Ovid and Cochrane Library, Web of Science, ScienceDirect Journals (Elsevier), Scopus (Elsevier), OneFile (Gale) followed the following steps: - search for mesh terms: *Lymphedema*, *Lymphatic System*, *Diagnosis*, *Treatment*, and *Bioimpedance*, and - use of boolean "and" between mesh terms and "or" among historical findings. All references are registered in EndNote.

Study Selection and Risk of Bias in Each Study

Two independent reviewers performed research and study selection. The data extraction was performed by reviewer 1 and fully reviewed by reviewer 2. A third investigator decided some conflicting points and made the final decision to choose the articles. Only studies reported in Portuguese and English were evaluated. The Cochrane instrument was adopted to assess the quality of included studies (Figure 1).

RESULTS AND DISCUSSION

It was found that there are several methods of assessing body composition based on different principles and body models, which allow characterizing body composition in a specific way, differentiating the various body segments, or in a global and undifferentiated manner [15-18]. There is also another method of evaluation, however, it presents a better practical application and lower financial cost, and can be used in field research or clinical study, especially bioimpedance [19].

About 90% of the cases, the diagnosis of lymphedema is established based on anamnesis. However, in some patients, especially when there are no associated risk factors or there are comorbidities to compete for edema, such as obesity, venous insufficiency, concomitant infections, the diagnosis may not be evident. In these cases, the use of complementary diagnostic tests, such as bioimpedance, may provide important information [19].

Also, in the case of primary lymphedema resulting from abnormalities in lymphatic system development during lymphangiogenesis, bioimpedance would not be required. In the case of secondary lymphedema resulting from obstruction or dysfunction of the lymphatic system, acquired, usually due to infectious disease, neoplastic obstruction or treatment associated with neoplastic disease (lymphadenectomy, radiotherapy) and inflammatory diseases, bioimpedance can be a great diagnostic resource [19].

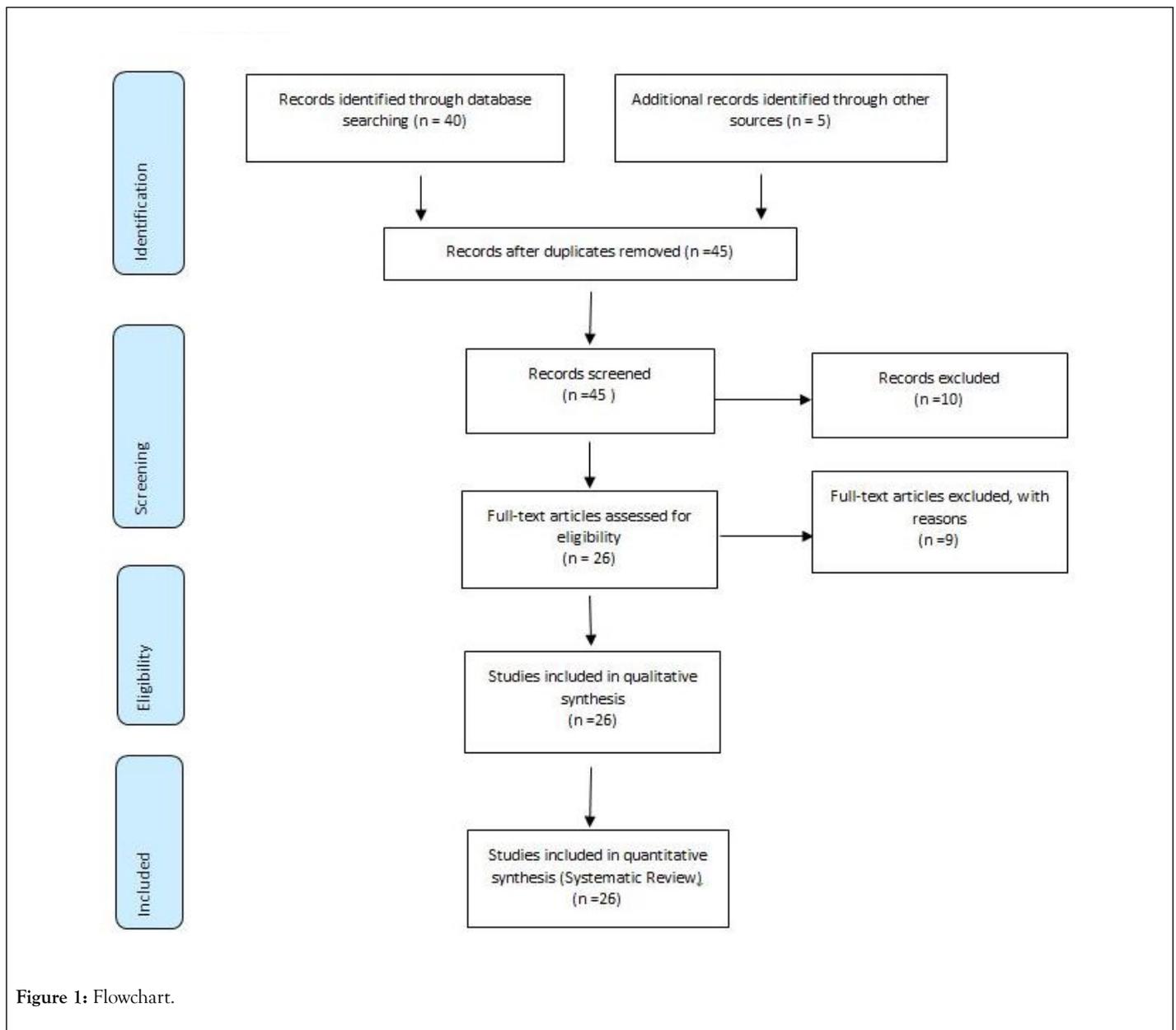
Bioimpedance is a non-invasive, painless and relatively accurate method of body evaluation. This method consists of the passage of a high-frequency, low-amplitude electric current. The measurement of body fluids is based on the fact that the fat-free mass contains electrolytes and acts as a conductor, while body fat is relatively free of ions and acts as an insulator. It is important to comment, that the bioimpedance device can provide values of fat mass, lean mass, body fluids and more characteristics such as sex, age, weight, and height [20-22]. In addition to these features, there is an advantage of bioimpedance, this method separately measures the intracellular and extracellular volumes of each body segment, and has been currently used in lymphedema. It is worth mentioning that bioimpedance can be performed before and after the treatment of lymphedema [23].

Based on this, a study has shown that bioimpedance is a reliable method for the evaluation of lymphedema, and the volume of the homolateral upper limb is associated with the amount of water in women with lymphedema secondary to the treatment of breast cancer [2].

Another study established normatively determined bioimpedance thresholds for unilateral upper limb lymphedema of the male sex. These thresholds should now be used to improve the early detection of unilateral lymphedema of the upper limbs [3].

It was observed in the studies Pereira de Godoy et al. [24], the research works with bioimpedance and lymphedema. The authors studied 13 (thirteen) patients between the ages of 46 and 57 years; all patients with arm edema. According to Godoy et al., Lymphoedema was confirmed by bioimpedance. In this study, the authors used diosmin together with hesperidin at the beginning of lymphedema to control arm swelling and, after treatment, the arm was again evaluated by bioimpedance. As a result, significant reductions in limb volume were detected ($p < 0.04$). It was observed that bioimpedance was able to detect body volumes before and after treatment.

The use of bioimpedance for the diagnosis of lymphedema in obese and non-obese patients was observed in the studies of Fátima Guerreiro Godoy, et al. [22]. The authors measured the patients' interstitial volumes, in addition to the measurement, the bioimpedance was able to analyze the patients' body fat, showing the effectiveness of bioimpedance for the measurement of body fluids and body fat.



In studies by Brigidio et al. [23], 14 patients with lower limb lymphedema were evaluated and treated. Patients were submitted to a continuous session of 2 (two) hours of mechanical lymphatic drainage through the RAGodoy® device. The measurement of lymphedema, as well as its response to treatment, was made by bioimpedance performed immediately before and after mechanical lymphatic drainage. As a result, a statistically significant reduction ($p < 0.0001$) was observed. In this study, bioimpedance was shown to be able to analyze fluids before and after intensive lymphedema treatment.

According to Deminici and Rosa [23] and Jaffrin [24], bioimpedance is preferable for the measurement of interstitial fluids especially extracellular fluid and also to measure body fat mass. For these authors, bioimpedance is being accepted in nutrition, hemodialysis, gerontology and also in sports medicine.

It is important to highlight the early diagnosis of the disease through bioimpedance, and thus, provide the patient with a

more useful treatment [25,26]. Therefore, bioimpedance is a method that can be used as a clinical and therapeutic diagnosis in lymphedema, since it is possible to determine, quantify the degree of accumulation of the fluid at the corporal end with lymphedema.

Risk of Bias

Considering the Cochrane tool for risk of bias, the overall evaluation resulted in 7 studies with high risk of bias and 2 studies with uncertain risk. The domains that presented the highest risk of bias were related to number of people involved in the studies, because some studies presented statistical results with a sample size of 10 or 15 patients, and this does not represent security in the statistical response. Also, the type of study design, as well as presence or absence of a declaration of conflicts of interest, because some studies did not follow a randomized controlled study.

CONCLUSION

Bioimpedance is an indicated method for evaluating the composition of interstitial lymphedema volumes before and after therapy sessions, either as a drug or as an intensive treatment of lymphedema. Therefore, bioimpedance is used to evaluate the clinical and therapeutic follow-up of patients with lymphedema.

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