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Medical Policy Manual

Topic: Bioimpedance Devices for Detection and Management of Lymphedema

Date of Origin: April 2011

Section: Durable Medical Equipment

Last Reviewed Date: June 2014

Policy No: 82

Effective Date: September 1, 2014

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Secondary lymphedema may develop following surgery for breast cancer. Bioelectrical impedance (bioimpedance) is being studied as a diagnostic test for lymphedema, particularly for early detection of "subclinical" disease.

Background

Secondary lymphedema of the upper extremity may develop following surgical treatment for breast cancer; it has been reported in approximately 25 to 50% of women following mastectomy. This can be a chronic, disfiguring condition. It results from lymphatic dysfunction or disruption and can be difficult to accurately diagnose and manage. One challenge is identifying the presence of clinically significant limb swelling through simple noninvasive methods. Many techniques have been used for documenting lymphedema including measuring differences in limb volume (volume displacement) and limb circumference. A number of newer techniques are being evaluated, including bioimpedance with use of bioimpedance spectroscopy (BIS) analysis, which uses resistance to electrical current in comparing the composition of fluid compartments. BIS is based on the theory that the amount of opposition to flow of electric current (impedance) through the body is inversely proportional to the volume of fluid in the tissue. In lymphedema, with the accumulation of excess interstitial fluid, tissue impedance decreases.

The detection of subclinical lymphedema, that is, the early detection of lymphedema before clinical symptoms become apparent is another area of study. Detection of subclinical lymphedema (referred to as Stage 0 lymphedema) is problematic. Subclinical disease may exist for months or years before overt edema is noted. This approach generally involves comparison of preoperative with postoperative measurements, since existing differences between upper extremities (like the effects of a dominant extremity) may obscure early, subtle differences resulting from the initial accumulation of fluid. Bioimpedance has been proposed as one diagnostic test for this condition. Those who support the approach to diagnose subclinical disease believe that early treatment of subclinical lymphedema should result in less severe chronic disease.

Regulatory Status

One bioimpedance device is the ImpediMed L-Dex™ U400 cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process in 2007 and in 2008. According to the FDA letter, the device is "to aid in the clinical assessment of unilateral lymphedema of the arm in women. The device is not intended to diagnose or predict lymphedema of an extremity."

MEDICAL POLICY CRITERIA

Devices using bioimpedance (bioelectrical impedance spectroscopy) are considered **investigational** for use in the diagnosis, surveillance, or treatment of patients with lymphedema, including use in subclinical secondary lymphedema.

SCIENTIFIC EVIDENCE

Assessment of a diagnostic technology typically focuses on the following three parameters: 1) technical performance; 2) diagnostic performance (i.e., sensitivity, specificity, and positive and negative predictive value) in appropriate populations of patients; and 3) demonstration that the diagnostic information can be used to improve patient outcomes (clinical utility). While in some cases, tests can be adequately evaluated using technical and diagnostic performance, when a test identifies a new or different group of patients with a disease, randomized controlled trials (RCTs) are needed to demonstrate impact of the test on the net health outcome.

Literature Appraisal

Most studies reported on secondary lymphedema of the upper extremity following surgery for breast cancer. The generally accepted approach to the diagnosis of lymphedema uses measurement of volume displacement and/or limb circumference. Most studies related to diagnosis involve these approaches. In contrast, the literature regarding bioelectrical impedance analysis is limited.

Technical Performance

Technical performance of a device is typically assessed with two types of studies, those that compare test measurements with a gold standard and those that compare results taken with the same device on different occasions (test-retest). While there is no absolute gold standard for diagnosis of lymphedema,

the de facto gold standards are limb volume and/or limb circumference. These measurements have been judged to be both valid and reliable.

A 2010 publication by Czerniec and colleagues reported on measurement of lymphedema in a small group of patients, 33 with lymphedema and 18 without.[1] The aim of this study was to determine the relationship between physical methods of measuring lymphedema and self-reported swelling. Measurement techniques included self-report, bioimpedance spectroscopy, perometry, and the truncated cone method. The authors noted that the physical measurement tools were highly reliable with high concordance (0.89 to 0.99, respectively). In this study, self-report correlated moderately with physical measurements (0.65 to 0.71, respectively) and was moderately reliable. The authors concluded that lymphedema assessment methods are concordant and reliable but not interchangeable.

Diagnostic Performance

Diagnostic performance is evaluated by the ability of a test to accurately diagnose a clinical condition in comparison with the gold standard. The sensitivity of a test is the ability to detect a disease when the condition is present (true positive), while specificity indicates the ability to detect whether disease exists in patients who are suspected of disease but who do not have the condition (true negative). Evaluation of diagnostic performance, therefore, requires independent assessment by the two methods in a population of patients who are suspected of disease but who do not all have the disease.

Technology Assessment

A technology assessment on the diagnosis and treatment of secondary lymphedema, performed under contract from Agency for Healthcare Research and Quality (AHRQ) by the McMaster University Evidence-based Practice Center, was released in May 2010.[2] The assessment identified eight studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. The two studies that evaluated bioimpedance devices are briefly described below:

- In a study from Australia, Cornish and colleagues followed 102 patients after treatment for breast cancer.[3] Twenty patients developed lymphedema in the 24 months follow-up period, and in these 20 cases, multi-frequency bioelectrical impedance analysis (MFBIA) predicted the onset of the condition up to 10 months before the condition was diagnosed clinically. Estimates of the sensitivity and specificity were both approximately 100%. At the time of detection by MFBIA, only one of the patients had a positive test result from the total limb volume determined from the circumferential measures.

- In another study from Australia, Hayes and colleagues noted that the point prevalence of lymphedema varies according to the approach to diagnosis.[4] In this study, lymphedema status was assessed at 3-month intervals between 6 and 18 months post-surgery in a sample of Australian women with unilateral, invasive breast cancer, using three methods: bioimpedance spectroscopy (BIS), difference between sum of arm circumferences (SOAC), and self-report. Depending on the method, point prevalence ranged between 8 to 28%, with 1 in 5 to 2 in 5 women experiencing lymphedema at some point in time. According to the technology assessment, the sensitivity and specificity of bioimpedance compared to SOAC was 42% and 88%, respectively and the sensitivity and specificity of bioimpedance compared to self-report was 61% and 59%, respectively.

The technology assessment concluded that in contrast to information about the techniques of circumferential measurement and volume displacement, “there is too little evidence to draw conclusions

about the reliability of …bioimpedance." The report also noted that the studies do not allow conclusions about the potential impact of timing of the initial intervention.

Nonrandomized Studies

Only one comparative trial has been published since the 2010 TEC assessment. In 2011 Smoot and colleagues reported on diagnostic test characteristics including sensitivity, specificity, and area under the receiver-operating-characteristic (ROC) curve for a number of tests used in the diagnosis of breast cancer-related lymphedema.[5] For this study, a total of 141 women were classified as having (n=70) or not having (n=71) breast cancer-related lymphedema (BCRL) based on past diagnosis by a health care provider. Areas under the curve for a number of bioimpedance measures and volume measures were in the 0.79 to 0.88 range, with overlap in confidence intervals. Given questions about the standard used for diagnosis and apparent lack of patients with subclinical lymphedema, this study provided little new information.

Similarly, a 2012 retrospective review of bioimpedance analysis in 64 women who underwent surgery for breast cancer failed to include a reference standard test for comparison. In addition, the authors did not report on diagnostic performance (i.e., sensitivity and specificity).[6] Because of these study design limitations, conclusions on the diagnostic performance cannot be reached.

Clinical Utility

Clinical utility is evaluated by assessing the evidence for the ability of a test to be used in patient management to improve health outcomes. Randomized trials comparing the health outcomes of patients managed with versus without the use of bioimpedance are needed to demonstrate the impact of the test on net health outcome. No such randomized controlled trials were identified.

A related question is whether early detection and treatment of subclinical lymphedema using a bioimpedance device or another detection method improves health outcomes. The literature on treatment shows variability among studies regarding response to therapy for secondary lymphedema. Some studies found that mild disease was more responsive to treatment; other studies did not. Similarly, when the duration of symptoms was reported, there was no clear relationship between duration of the edema and response to treatment.

- A study by Stout Gergich and colleagues is frequently cited as support for early detection and treatment of subclinical lymphedema.[7] In this study, lymphedema was identified in 43 of 196 women who participated in a prospective breast cancer morbidity trial. Limb volume was measured preoperatively and at 3-month intervals after surgery using perimetry (another evolving technique). If an increase of greater than 3% in upper limb volume developed compared with the preoperative volume, then a diagnosis of lymphedema was made and a compression garment intervention was prescribed for 4 weeks. Statistical analysis was a repeated-measures analysis of variance by time and limb ($p<0.001$) comparing the lymphedema cohort with an age-matched control group. In this study, the time to onset of lymphedema averaged 6.9 months postoperatively. The mean (+/-standard deviation [SD]) affected limb volume increase was 83 mL (+/-119 mL) at lymphedema onset compared with baseline. Of note, clinical lymphedema is generally felt to be apparent when 200 mL of fluid accumulates. After the intervention, a statistically significant mean 48 mL (+/-103 mL) volume decrease was realized. The mean duration of the intervention was 4.4 weeks. Volume reduction was maintained at an average follow-up of 4.8 months after the intervention. The authors concluded that a short trial of compression garments effectively treated subclinical lymphedema.

This study does not answer the key question, that is, whether net health outcome was improved by early intervention. In addition, the role of novel diagnostic testing compared to the use of the de facto gold standard tests (limb volume or circumference) also needs to be evaluated.

- In a study from Europe involving 55 women who had breast cancer and axillary node dissection, Boccardo and colleagues evaluated a preventive protocol for lymphedema.[8] The preventive group had volumetric (arm volume) measurements performed preoperatively and at 1, 3, 5, 12, and 24 months postoperatively. The protocol for this group included principles to minimize lymphedema risk, lymphoscintigraphy preoperatively and at 6 months postoperatively, and early management of the condition once identified. Clinically significant lymphedema was an increase of at least 200 mL from the preoperative difference between the two arms. Assessments at 2 years were completed for 89% of the 55 women who were randomly assigned to either preventive group or control. Of the 49 who were measured at 2 years, 10 (21%) were identified with secondary lymphedema with an incidence of 8% in the preventive group and 33% in controls. The authors noted that these prophylactic strategies appear to reduce the development of secondary lymphedema and alter its progression. This was a relatively small study, and the various interventions used may have each played a role in the outcome for this study.

Clinical Practice Guidelines

There are currently no clinical practice guidelines from U.S. professional associations that recommend the use of bioimpedance devices for early detection or treatment of lymphedema.

Summary

Current evidence is insufficient to permit conclusions about the technical performance and diagnostic validity of bioimpedance testing in the diagnosis of lymphedema. In addition, there are no data that demonstrate the impact of bioimpedance testing on clinical outcomes (clinical utility). Thus, based on the current scientific evidence and because the impact on net health outcome is not known, use of bioimpedance in the diagnosis or management of patients with known or suspected lymphedema is considered investigational.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	0239T	Bioimpedance spectroscopy (BIS), measuring 100 frequencies or greater, direct measurement of extracellular fluid differences between the limbs
HCPCS	None	