

Resource Requirements for Breast Surgery in Low and Middle Income Countries

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Globally, breast cancer is the most common cancer among women, comprising 23% of all female cancers that are newly diagnosed in more than 1.1 million women each year.¹ Breast cancer is the most common cause of cancer-related death among women worldwide, with case fatality rates highest in low- and middle-income countries (LMCs). Despite the common misconception that breast cancer is predominantly a problem of wealthy countries, 55% of breast cancer deaths each year in fact occur in developing rather than developed countries.² More than 411,000 deaths each year result from breast cancer annually, accounting for more than 1.6% of female deaths from all causes.³ By 2010, the annual global burden of new breast cancer cases will rise to 1.5 million with an ever-increasing majority will be from LMCs.² Approximately 4.4 million women diagnosed with breast cancer in the last 5 years are currently alive, making breast cancer the single most prevalent cancer in the world.¹

Guideline development for breast cancer in LMCs

While evidence-based guidelines outlining optimal approaches to breast cancer detection, diagnosis, and treatment have been well developed and disseminated in several high-resource countries such as the U.S., these guidelines may be inappropriate to apply in LMCs for numerous reasons including inadequate personal resources, limited health care infrastructure, lack of pharmaceuticals, and cultural barriers. Hence, there is a need for clinical practice guidelines oriented toward LMCs, specifically considering and adapting to existing health care resources. The Breast Health Global Initiative (BHGI) has developed evidence-based, economically feasible, and culturally appropriate guidelines that can be used in nations with limited health care resources to improve breast cancer outcomes.⁴ Modeled after the approach of the National Comprehensive Cancer Network (NCCN), BHGI created and applied a consensus panel process now formally endorsed by the Institute of Medicine (IOM)⁵ to define resource-sensitive guidelines for breast cancer early detection,⁶ diagnosis,⁷ treatment,⁸ and health care systems,⁹ as related to breast health care delivery in LMCs. The BHGI guidelines are intended to assist ministers of health, policymakers, administrators, and institutions in prioritizing resource allocation as breast cancer treatment programs are implemented and developed in their resource-constrained countries.

Several key observations were made through the BHGI resource-stratified guidelines. Breast cancer outcomes correlate with the degree to which 1)

cancers are detected early, 2) cancers can be diagnosed correctly, and 3) proper multimodality treatment can be provided in a timely fashion. Cancer prevention through health behavior modification may influence breast cancer incidence in LMCs.¹⁰ Diagnosing breast cancer at earlier stages is predicted to reduce breast cancer mortality. Programs to promote breast self-awareness and clinical breast examination and resource-adapted mammographic screening are important early detection steps.⁶ Screening mammography has been shown to reduce breast cancer mortality, but is cost prohibitive for most LMCs. Breast imaging, initially with ultrasound and, at higher resource levels with diagnostic mammography, improves preoperative diagnostic assessment and permits image-guided needle sampling.⁷ Comprehensive multimodality treatment including surgery, radiation, and systemic drug therapies, must be in place for the benefit of early cancer detection to be realized.⁸

The role of surgical excision in breast cancer diagnosis

While surgical excision for diagnosis can be used when alternatives are unavailable, needle sampling is highly preferable.^{11, 12} Under no circumstances should mastectomy be considered an acceptable method for tissue “sampling”.¹¹ Fine needle aspiration biopsy (FNAB) is recognized to be the most cost effective procedure with the shortest turnaround time.¹³ The choice of sampling procedures (FNAB, core needle biopsy or excisional biopsy) should be based on the availability and access to cytopathologists/pathologists in each medical community, and the training and experience of the available pathology specialists.¹⁴

Surgical treatment for breast cancer in LMCs

The ability to perform a modified radical mastectomy (MRM), which includes surgical excision of the breast together with a level I/II axillary lymph node dissection, is considered a basic requirement for the management of patients with early stage breast cancer. The resources for surgical therapy are typically available in most medical settings that provide minimally advanced health care (Table 1). The availability of radiation therapy allows for consideration of breast conserving therapy, post-mastectomy chest wall radiation, and for the palliation of painful or symptomatic metastases.¹⁵

Lymph node metastasis is the single most important factor in assessing breast cancer prognosis and planning systemic therapy. Lymphadenectomy has therapeutic benefit for breast cancer patients, since axillary dissection renders regional control of axillary disease.¹⁶⁻¹⁸ The ability to perform a proper axillary dissection is a basic technique with which surgeons must be fully familiar in order to be able to provide comprehensive breast surgical care to breast cancer patients. However, lymph node dissection portends significant morbidity, with little or no therapeutic (as opposed to diagnostic) benefit if the nodes prove to be negative for cancer. Sentinel lymph node (SLN) biopsy, while developed in the context of high-income countries, actually can be used by breast surgery teams in lower income settings at low cost, when the technique is restricted to the use of blue dye without radiotracer.¹⁹

Surgical pathology as a key resource for breast surgery

Quality surgical pathology is critical to breast program function.^{7, 14} The availability of predictive tumor markers, especially ER testing, is critical to proper selection of cancer therapy when endocrine therapies are available, although quality assessment of immunohistochemical (IHC) testing is important to avoid false negative results. Interdisciplinary communication underlies the basis of success for breast diagnostic programs at all economic levels. Furthermore, the interaction of the pathologist with the radiologist and the surgeon (interdisciplinary team collaboration) is critical in the examination and reporting of the pathology specimen, since the clinical situation in which the specimen was obtained can markedly influence the significance of certain pathological findings, and in the case of cancer, can be critical in determining accurate tumor staging.

Management of locally advanced breast cancer

Despite the fact that breast cancer is the most common cancer among women in LMCs, these countries commonly lack early detection programs for breast cancer. As a result, women in LMCs commonly present with locally advanced breast cancer. Recent data shows that locally advanced breast cancer (LABC) and metastatic breast cancer are the most common stages at presentation, 60-80% of cases, in most LMCs.²⁰⁻²² While the incidence of LABC has decreased significantly in developed countries with enhanced and maximal resources due to widespread education and increasing utilization of screening mammography.²³ LABC remains a daily challenge for oncologists in LMCs where limitations to proper management include also lack of local data, cultural circumstances, and weak inefficient health care systems.

Preoperative chemotherapy is the preferred primary therapy for LABC, because it allows early assessment of sensitivity to treatment as well as breast conservation.²³ Clinical assessment of chemosensitivity may be particularly helpful, because emerging data suggests that there could be differences in host metabolism of systemic treatment agents—tamoxifen, alkylating agents, taxanes—on genetic bases, with associated efficacy and toxicity differences among genetically different populations.^{24, 25} Research specifically directed at differences among groups in response to systemic therapy may be warranted.²⁶ While the preferred initial treatment of LABC is systemic therapy, if optimal chemotherapy and evaluation are not available, then primary MRM is acceptable. However, it should be recognized that without systemic therapy, surgery alone for LABC is unlikely to improve outcome, given the high likelihood of systemic relapse, so the role of MRM without adjuvant treatment for LABC should be viewed primarily as palliative therapy.

After responding to systemic therapy, most LABC patients will require an MRM followed by radiation therapy.²⁷ Locoregional therapy decisions should be based on both the pretreatment clinical extent of disease and the pathologic extent of the disease after chemotherapy. Accordingly, physical examination and imaging studies that accurately define the initial extent of disease are required before treatment.²⁸ The success of breast conservation after preoperative chemotherapy depends on careful patient selection and achieving negative surgical margins. Adjuvant breast radiation is indicated for all patients treated with breast conservation. For patients treated with mastectomy, chest-wall and regional nodal radiation should be considered for those who present with clinical stage III disease or have histologically positive lymph nodes after preoperative chemotherapy.²⁸

Metastatic and inflammatory breast cancer should be initially managed with preoperative therapy irrespective of resource level. Standard preoperative therapy includes anthracycline-based chemotherapy. The addition of sequential taxane after anthracycline-based chemotherapy improves pathological responses and breast-conservation rates, though may not improve survival. The combination is considered appropriate treatment at the enhanced and maximal level; however, costs and lack of clear survival benefit do not justify its use at limited resource levels. CMF combination chemotherapy is less potent than anthracycline and taxanes, but may be used in its classical schedule in LMCs because of lower costs and lesser complications. The role for preoperative endocrine therapy remains to be better defined, but appears to be feasible and acceptable in elderly women.²³

Training in breast surgery in LMCs

While the MRM is considered fundamental surgical training in high-income countries, surgeons from LMCs may have had less exposure to the procedure and may not be knowledgeable about the operation's proper technical execution. A retrospective review of patients referred from outside institutions to Tata Memorial Hospital in Mumbai, India found that of 424 who had undergone "therapeutic" surgical interventions, 191 (45%) were judged to have incomplete surgery. Of these, 153 patients underwent completion revision surgery and 123 had residual axillary nodes including 64 patients (52%) with metastatic lymph nodes found to have been left behind in the axillary bed.²⁹ Thus, surgical training in LMCs needs to address education regarding these fundamental oncologic surgical procedures.

Quality control measures and process metrics as tools for decision making

While resource stratified guidelines may provide a framework for systemic improvement in cancer care delivery, these guidelines are useful only if they are implemented and if that implementation success is in turn measured. Quality control measures need to be integrated into cancer care programs at all levels of early detection, diagnosis and treatment. Focusing efforts at improving performance in problem areas assures efficient resource utilization and maximizes positive impact. Non-punitive reporting of errors is a key step in improving patient safety. Proper methodology for defining quality improvement initiatives must be considered, and adapted to existing resources.³⁰ Without metrics, it is difficult to determine programmatic success.

Process metrics are also useful tools for tracking progress and informing future decisions by policy makers. Carefully selected process metrics can be collected without excessive effort or cost and can be used to measure the effectiveness of a facility or country's ability to detect, diagnose and treat cancer. Generally, the

sophistication of metrics will increase with the level of resources. Certain metrics, such as the rate of breast conserving surgery for operable breast cancer, can be used at many levels of resources as a benchmark the target for which will change as resources levels increase.⁸

Among the most fundamental breast cancer metrics for LMCs is TNM stage at diagnosis. The fraction of patients who have early versus late stage disease at initial biopsy-proven breast cancer diagnosis is a simple and direct measure of breast cancer early detection in a population.⁹ In India, as many as 70% of women with breast cancer have locally advanced (stage III) or metastatic disease (stage IV) at presentation.³¹ The rate of late stage diagnosis is a guide to health care ministers regarding the need to make systemic chemotherapy widely available. This statistic also provides a financial justification for improving early detection of breast cancer, since late stage disease is more costly to treat with decreased likelihood of improving cancer-related longevity.²³ In many LMCs, collection of even rudimentary measurements will be difficult. Despite these difficulties, LMCs should actively engage in creating and employing metrics that can be easily integrated into existing practices in order to optimize outcome and determine best strategies for improving breast cancer outcome in LMCs.

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Tables

Table 1. Breast cancer surgery checklist⁸

Therapy	Strengths	Weakness	Required sources
Modified radical mastectomy (MRM)	Rapid treatment Curative for early breast cancer Technology to perform widely available	Disfiguring.	Staff <ul style="list-style-type: none"> • Surgeon • Anesthesiologist • Pathologist • Nursing • Physiotherapist • Medical Social Worker /Counselor Surgical resources <ul style="list-style-type: none"> • Operating theater • Anesthetics • Post-operative care system
Breast conserving surgery with axillary dissection	Rapid surgical treatment	Technically demanding Not appropriate for all patients Requires ability to assess margin status by breast imaging and pathology Requires application of post-operative radiation therapy as potentially curative therapy for breast cancer	Surgical staff and resources as above under MRM
SLN with blue dye	Allows for accurate identification of SLN Minimizes post-surgical morbidity in women with negative axillary lymph nodes	Requires experienced SLN team Rare allergic reactions	Staff <ul style="list-style-type: none"> • Experienced surgeon • Experienced pathologist
SLN with radiotracer	Allows for accurate identification of SLN Minimizes post-surgical morbidity in women with negative axillary lymph nodes	Requires experienced SLN team. Special handling of radiotracer	Staff <ul style="list-style-type: none"> • Experienced surgeon • Experienced pathologist Procedures, equipment, and facilities for radio tracer handling (nuclear medicine)

SLN:sentinel lymph node