

Review Article

Current Level of Evidence on Late Complications of Breast-Cancer Management in Democratic Republic of the Congo: Review of Literature

Jean Paul Muambangu Milambo^{1*}, Valery Kazadi Tshilombo², Leonidas Ndayisaba³, Tamuzi Jacques¹

¹Division of Health Systems and Public Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

²Unit of Infection Control and Prevention, Department of Global Health, Stellenbosch University, Cape Town, South Africa

³Department of Respiratory Intensive Care, Groote Schuur Hospital, Cape Town, South Africa

***Corresponding author:** Jean Paul Muambangu Milambo, Division of Health Systems and Public Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, 25 Norden Road, Parow 7500, South Africa. Tel: +27719953868; Email: Jeanpaulmilambo2@gmail.com

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Abstract

Breast Cancer Related Lymphedema (BCRL) is a significant long-term comorbidity associated with (BC) management. BCRL impacts significantly on physical, psychosocial and economic implications of BC survivors, as a result of lymphatic system dysfunction related to breast injury. Many modifiable and non-modifiable risk factors for BCRL were identified in literature; these have contributed to cure progress and advanced knowledge on BCRL diagnosis and management at clinical stage. However, most of these studies were conducted in developed countries with limited information on such predictors and successful management strategies within African settings. Therefore, this review was conducted to summarize the available evidence on BCRL risk factors, incidence and management pathway in Democratic Republic of the Congo.

Abbreviations

BIS	:	Bioimpedance Spectrometry
BCRL	:	Breast Cancer Related Lymphoedema
CDT	:	Complex Decongestive Therapy
DRC	:	Democratic Republic of the Congo
LE	:	Lymphoedema
MLD	:	Manual Lymphatic Drainage
MSEP	:	Medically Supervised Exercises program
ISL	:	International Society of Lymphology
HRQOL	:	Health Related Quality of Life
WHO	:	World Health Organisation
QOL	:	Quality of Life
ROM	:	Range of Motility

Introduction

There is increased number of breast cancer survivors globally because of population growth and advanced in aging. It is estimated that approximately 1.7 million new cases of breast cancer cases diagnosed in 2012; accounting about 12% of incidence of all new cancer cases and 25% of all cancers in women. BC is classified the 5th cause of mortality among women [1]. In several countries, with advanced oncological techniques developed to manage breast cancer; the survivorship rate of early detection of BC was increased from 80% to 90%, following to 25 percent for BCs detected at advanced stage [1,2]. BC is more prevalent in developed countries, but estimated 55% of breast cancer deaths occur in lower and developing countries [1]. A relative 5 - years survivorship have been improved from 80% to 90% in developed countries, to 60% in developing countries, to below 40% in low income countries; within African continent, it may be as low as 11,99% [2].

Democratic Republic of the Congo (DRC) is a low income country located in middle Africa with life expectancy at birth

of total 52 years; males= 50 years and females=53 [1]. BC mortality profile in DRC reported by World Health Organization (WHO) in 2014 was 16.00%, Age Standardized Incidence Rate (ASIR) of 4.570 per 1000 females at risk [1]. The recent data demonstrate that 60% of population living in DRC are women; the most common cancers in prevalence and mortality for women are cervical cancer and BC (Figure 1 and 2 are attached at the bottom of the manuscript show the burden of cancers in DRC), yet there is no screening program for early detection of cancers [1]. A number of breast cancer patients are diagnosed at delayed stage of the condition and the prognostic is likely poor in most of the cases. Although BC treatment, includes surgery, radiation therapy, chemotherapy and hormonal therapy, have improved the outcomes resulting to prolonged survivorship; these techniques have also led BC survivors to potentially suffer from different comorbidities [3]. Many studies have demonstrated that BCRL is the most prevalent comorbidity associated with BC treatments [4-10]. Lymphoedema (LE) is the stasis of lymphatic fluid in interstitial tissues as result of dysfunction related to lymphatic system drainage of protein-rich liquid [5]. The consequences of lymphatic fluid stasis can lead to edema and hypoxia which are more observed in peripheral tissues [5]. The affected area can become swollen and distorted in shape [6-10]. This can result in pain, disfigured body parts, heaviness, discomfort, impairment of movement and it impacts on daily activities [11-14]. The details on international Classifications of Lymphoedema and the common symptoms can be found in International Society for Lymphoedema (ISL) guideline [7]. BCRL decreased the Health Related quality of life (HRQOL) and it is a life-long complication and considered the major sequelae associated with BC management [8]. Given that high incidence of BC in DRC with advanced techniques to manage BC; the comorbidities associated with BC management such as BCRL should be increased. However, there is no standardized BC guideline in DRC, the true prevalence and incidence of BC is not known because of lack of cancer registry in each province, data provided in this paper cannot be representative to all DRC. There is a Scarce of data on incidence, risk factors and management of BCRL in African countries such as DRC. This review aims to inform all stakeholders on awareness of BCRL among breast cancer survivors in DRC; so the evidence based healthcare approaches can be developed to mitigate BCRL occurrence.

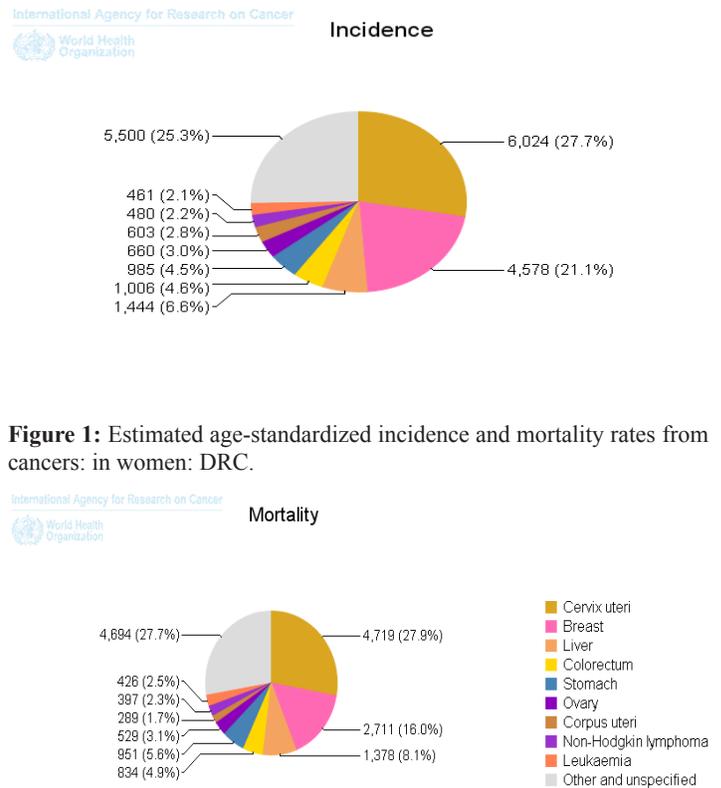


Figure 1: Estimated age-standardized incidence and mortality rates from cancers: in women: DRC.

Figure 2: Standardized Mortality rate of cancers in DRC.

Figure 1 and Figure 2: Types of cancer mortality and incidence rates are presented at the right side of the figures; each color corresponds to specific cancer type: incidence rates and mortality rates.

Methods

MEDLINE, EMBASE, PubMed and Cochrane breast cancer registry were searched to identify the published articles focused on prevalence, incidence, risk factors and management of BCRL in DRC. MeSH term included: (“breast cancer lymphedema”[MeSH Terms] OR (“Breast”[All Fields] AND “cancer”[All Fields] AND “lymphedema”[All Fields]) OR “breast cancer lymphedema”[All

Fields] OR (“breast”[All Fields] AND “cancer”[All Fields] AND “related”[All Fields] AND “lymphedema”[All Fields]) OR “breast cancer related lymphedema”[All Fields]) AND (“democratic republic of the congo”[MeSH Terms] OR (“democratic”[All Fields] AND “republic”[All Fields] AND “congo”[All Fields]) OR “democratic republic of the congo”[All Fields])) AND DRC [All Fields].

Current Status of Knowledge

One case report of BCRL was reported in the province of Katanga; a female BCRL patient was identified in Hospital of Lubumbashi after 2 years post mastectomy and actually on Tamoxifen 20 mg/daily [15]. The management of BCRL of this patient was not reported on the paper and the authors concluded that there is no evidence based study on this condition in our country, there is lack of an appropriate organized service to manage this type of complications and the prognosis is poor [15]. Although the incident cases are common in DRC; but there is lack of knowledge related to diagnosis and management of BCRL in DRC. Furthermore, financial concern, scare on appropriate materials related to socio-economic characteristics of the country, these impact in reducing in QOL and survivorship of BCRL patients [15].

Our review shows that there is lack of data on risk factors, incidence and management pathway of BCRL in DRC. A number of barriers were identified through the case report; these including lack of awareness on BCRL risk assessment, lack of healthcare worker’s knowledge in management of BCRL, lack of national guideline and policy for cancers prevention and control, lack of specialized facilities in lymphedema management and socio-economic determinants of the country are more concerned [15]. This condition need awareness of health systems providers and policy makers for it prevention.

The incidence of LE among women undergoing BC treatment varies from 6% to 83% in literature [6]; the pooled incidence rate of LE reported in recent systematic review was 40% in 2010 [9]. BCRL incidence increases with the time since the diagnosis period. The incidence rates of LE can be under or over reported because of lack of standard protocol for diagnosis and measurement tools [9]. Further, the incidence of BCRL depends on the number of nodes removed during the breast surgery, types of BC treatment and the

techniques used to measure LE volume [13].

There is a possible inaccuracy related to risk factors of the BCRL in many studies. The notable predictor of LE is extended BC surgery; this including axillary lymphatic node dissection and number of lymphatic nodules removed [9]. Other study has revealed that radiotherapy is associated with increased risk of developing BCRL [9], but other studies did not find the association between LE and radiation therapy [13,14]. This contradiction may be partially related to radiation doses used to treat the patients [9]. Of the clinical parameters associated with high risk to develop BCRL, the elevated Body Mass Index (BMI>25), being obese (BMI>30) are the most consistent risk factors to LE [13,14]. In addition, positive lymphatic nodes and advanced stage of diseases are also reported in the review [15]. Moreover, recent development in molecular analysis demonstrated that congenital lymphatic system dysfunctions can be associated with various candidate genes to be established in early onset of LE for it prevention or management [15]; these including genes FLT4, FOXC2, HGF, GJC2 and SOX-18 [15]; American African women has also been reported being associated with BCRL risk factors in one pathway study [14]. In contrast to one review, such association was not statically significant. Growing in age, high level of education and socioeconomic indications were found to be both risk factors and risk reduction in some studies [9]. ISL purposes to promote all activities associated with knowledge translation in the field of lymphedema management, establishes relationship between researchers and clinicians working in the field of lymphology as well as allied healthcare workers [7]. ISL provides the platforms to exchange the ideas with different experts in lymphology field and collaborate with other national and international organizations [7]. Further, ISL also organizes international congresses yearly and postgraduate training in lymphology and wound care [7].

Various methods can be found in literature which can be used to diagnose or to measure BCRL and its incidence varies according to the methods used, such as circumferential limbs measurements, perometry, Bioimpedance Spectrometry (BIS) and water displacement [9,16]. BIS is considered gold standard for LE diagnosis [14]; although; the review advocates that perometry should be more accurate than BIS, but the level of evidence for perometry still need to be established [16]. Tables 1 and 2 at the bottom of the manuscript shows the most common symptoms considered for LE diagnosis and ISL staging of LE respectively.

The following questions are about your experiences with movement on your affected body side today or in the past three month. The word “affected” means the same body side(s) on which you received breast surgery or radiation.					
On which body side was your cancer treated? Right: <input type="checkbox"/> left: <input type="checkbox"/>					
Do you have limited movement of your affected ?	How severe?				
	NO=0	A little=1	Somewhat=2	Quite a bit=3	Very Severe=4
1. shoulder					
2. elbow					
3. wrist					
4. fingers					
The following questions are about symptoms in your affected arm, hand, breast, axilla (under arm), or chest today or in the past three month.					
How Severe?					
Have you had ___?	NO=0	A little=1	Somewhat=2	Quite a bit=3	Very Severe=4
5. swelling					
6. breast swelling					
7. chest wall swelling					
8. firmness					
9. tightness					
10. heaviness					
11. toughness or thickness of skin					
12. stiffness					
13. tenderness					
14. hotness/increased temperature					
15. redness					
16. blistering					
17. pain					
18. numbness					
19. burning					
20. stabbing					
21. tingling					
22. arm or hand fatigue					
23. arm or hand weakness					
24. pocket of fluid develop					
Fu, M.R. & Rosedale, M. Breast cancer survivors’ experience of lymphedema related symptoms. Journal of Pain and Symptom Management, (2009). 38(6), 849-859.					

Table 1: BCRL Risk Assessment.

Stage 0 (subclinical)	Swelling is not yet evident, despite the impaired lymphatic system.
Stage 1	Early fluid accumulation that subsides with limb elevation.
Stage 2	Swelling is constant and does not resolve using elevation, and pitting is evident.
Stage 3	Pitting may be absent, although trophic skin changes have developed.

Table 2: International Classification of Lymphedema: 2013.

LE does not have a curative treatment; the Complex Decongestive Therapy (CDT) is considered the standard care internationally for LE management but the level of evidence is not yet established for each component of this intervention [16,17]. CDT enhances limb functions, maintains arm volume, reduces swelling and pain, and minimize disfiguration of the body shape. It includes four components: Manual Lymphatic Drainage (MLD), compression sleeves, remedial limb and deep-breathing exercises to promote venous and lymphatic flow and patient self-care. There are 2 CDT phases: the intensive phase includes all 4 components provided by LE therapists; in maintenance phase or secondary phase of CDT, a patient practices MLD assisted by physiotherapists or a trained care giver and skin care to prevent infections; this last phase is life-long therapy [17]. Additionally, maintenance phase of CDT is challenged for the patients to monitor and practice self-care which is associated with noncompliance and can result to increase LE volume; recommended exercises purpose to restore Range of Motility (ROM) and to strength of affected limbs. There is inconsistency on exercise prescription and use of MLD; as the result there is lack of standardized exercise protocol for different stages of BCRL. Moreover, providing patients education on LE risk reduction among patients at risk was proved effective in improving a quality of life [17,18]. This risk reduction program including lifestyle interventions (eating healthy foods and participation in weekly regimen of supervised exercises) to be combined with CDT at maintenance phase of the treatment [19-23].

Conclusion

There is scarce of data on BCRL risk factors and management in DRC. No evidence based standardized guideline have been developed to date to assess the efficacy of a number of treatment options implemented in developed countries. More studies are needed to extend the knowledge, skills, and awareness of secondary lymphoedema throughout all the stakeholders.

BCRL is life-threatening condition associated with breast cancer management. Patient education on risk reduction strategies such as lifestyle, proactive risk factor managements,

and developing specialized services with acquainted healthcare providers in lymphoedema management pathway should improve patients HRQOL. Cancer registry and innovative clinical studies should be conducted to mitigate its occurrence.

The following recommendations are addressing to healthcare providers, researchers, policy makers and the funders:

- Organisation of undergraduate and postgraduate training in cancer rehabilitation, especially in physiotherapy.
- Provide evidence based research platforms to inform healthcare providers and patients on awareness of LE.
- Develop a national cancer clinical guideline and surveying database to inform all stakeholders on impact of BCRL.
- Develop the preclinical diagnosis (gene expressing) for lymphoedema prevention.
- Develop a palliative care conceptual framework for cancer rehabilitation and secondary lymphoedema.
- Collaborate with the national and internal experts in the field of cancer rehabilitation, research and management

What is Already Know on this Topic?

- BCRL is common side effects associated with breast cancer management, impacts on BC survivors in reducing health related quality of life worldwide.
- The healthcare providers should be able to identify onset symptoms of BCRL, provide patients education on BCRL risk reduction and refer patients to specialized service for compression therapy.
- Breast Surgery, radiation therapy, hormonal therapy, chemotherapy, age, menopausal status, high body mass index and genetic predispositions are the consistent risk factors for breast cancer related lymphedema development.

What This Study Adds?

- Many healthcare providers in DRC are not aware of risk factors and management of breast cancer related lymphedema.
- Complex Decongestive Therapy is the standard of care for lymphedema internationally, it comprises 4 components: manual lymphatic drainage, compression sleeves, decongestive exercises and self-care. In addition, many countries lack their own guideline for lymphedema such as DRC.
- There is no curative treatment for BCRL at clinical stage, genotyping is recommended for BCRL risk prediction among patients at highest risk.

Competing Interests: The authors declare no competing interest.

Authors' Contributions

1. Designing, search strategy, writing, critical appraisal, edition and collaboration with other experts.
2. Designing figures, tables and critical appraisal, edition and search strategy.
3. Designing figures, tables and critical appraisal, edition and proofreading.
4. Design, search strategy, writing and critical appraisal, edition and collaboration with other experts.

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