

# Incidence of and risk factors for arm lymphoedema following breast cancer treatment: a study in Ghana

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## Key words

Breast cancer, breast cancer-related lymphoedema, decorative tattoo lymphoedema, mastectomy tattoo

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## Abstract

**Objective:** This research aims to determine the incidence and risk factors of lymphedema after breast cancer treatment at the oncology unit of a hospital in Kumasi, Ghana. **Methods:** A descriptive, retrospective survey was used in this study. Breast cancer and lymphoedema-related variables were collected from the medical records of breast cancer patients. Data were analysed using descriptive statistics and chi-square tests. **Results:** Among 313 patients treated for breast cancer, 31 (9.9%) developed lymphedema after treatment. A chi-square test showed that axillary lymph node dissection was statistically a significant risk factor of lymphoedema (Chi-square test value = 7.055,  $P=0.008$ ). Radiation and late stage of breast cancer diagnosis may have contributed in development of lymphedema despite having  $P$  value  $> 0.05$ . Age, BMI and hypertension were also not associated with lymphoedema. **Conclusion:** This study provides evidence that the incidence of lymphedema was 9.9% with axillary lymph node dissection as a statistically significant risk factor of lymphedema. With the majority of breast cancer patients presenting with late-stage lymphoedema and also undergoing axillary lymph node dissection, lymphoedema will continue to be a problem in Ghana. Knowing the incidence and risk factors of lymphoedema not only assists in the early detection and effective management of the condition, but also provides baseline data for further research on lymphoedema in Ghana. Providing comfort and restoring function through lymphoedema management is important to maximising quality of life for patients. Lymphoedema management in late-stage breast cancer is particularly critical to comfort and quality of life.

**B**reast cancer-related lymphoedema (hereafter referred to as lymphoedema) is one of the most significant complications following breast cancer treatment (Paskett, 2008; Helyer et al, 2010). It is presumed to occur due to the body's inability to drain lymph fluid from the tissues due to damage to the lymphatic system after axillary surgery and radiation (Lawenda et al, 2009; Wanchai et al, 2016).

The diagnosis of lymphoedema is made following a detailed medical history, which includes time of onset, location of swelling, the course of progression of the swelling, pain and other symptoms (Hanks et al, 2006; Lacovara and Yoder, 2006; Lymphedema Framework, 2006; Lawenda et al, 2009; International Society of Lymphology, 2009; National Lymphedema Network (NLN) Medical Advisory Committee, 2011; Shigaki et al, 2013).

The incidence of lymphoedema following breast cancer treatment ranges from 5% to

60%, with onset of symptoms ranging from immediately after treatment to 30 years post-treatment (Loudon and Petrek, 2000; Clark et al, 2005; Sakorafas et al, 2006; Poage et al, 2008).

According to Bani et al (2007), Kocak and Overgaard (2000), Robegea et al (2015) and Kilbreath et al (2016), the reported incidence and severity of lymphoedema depends on the type of surgery, the use of radiotherapy and the number of lymph nodes removed. The incidence of lymphoedema also varies greatly depending on the extent of axillary treatment, the interval between axillary treatments and the methods used to define lymphoedema.

Several studies have shown that the onset of lymphoedema can occur at any time post breast cancer treatment (Loudon and Petrek, 2000; Clark et al, 2005; Sakorafas et al, 2006; Poage et al, 2008).

Several treatment-related factors have been associated with lymphoedema,

including type of breast surgery, extent of axillary dissection and addition of radiation therapy to the dissected axilla (Harris et al, 1991; 2000; Hanks et al, 2006; Dixo, 2009; Armer and Stewart, 2010; DiSipio et al, 2013; Kilbreath et al, 2016; Ribeiro Pereira et al, 2017; Safwat et al, 2017).

A preponderance of studies found a higher risk of lymphoedema related to axillary lymph node dissection, rather than sentinel lymph node biopsy (Blanchard et al, 2003; Golshan et al, 2003; Schijven et al, 2003; DiSipio et al, 2013). This may be attributed to less axillary dissection required when sentinel lymph node biopsies demonstrate negative pathologic results (Morrell et al, 2005; DiSipio et al, 2013).

Several studies demonstrate an increased lymphoedema risk in late-stage breast cancer disease with lymph node involvement (Schunemann and Willich, 1997; Park et al, 2008; Swenson et al, 2009; Ribeiro Pereira et al, 2017; Safwat et al, 2017). This may be the

**Table 1.** Risk and contributing risk factors of lymphoedema.

| <i>n</i> =31                           |          |                |                |             |                           |
|----------------------------------------|----------|----------------|----------------|-------------|---------------------------|
| <i>Profile of lymphoedema patients</i> | <i>N</i> | <i>Minimum</i> | <i>Maximum</i> | <i>Mean</i> | <i>Standard deviation</i> |
| Age prior to lymphoedema               | 31       | 30             | 78             | 52.81       | 10.901                    |
| BMI prior to lymphoedema               | 31       | 15.8           | 46.7           | 26.865      | 6.7490                    |
| Systolic blood pressure                | 31       | 100            | 170            | 134.19      | 17.659                    |
| Diastolic blood pressure               | 31       | 60             | 100            | 85.16       | 8.896                     |
| Radiation dose                         | 21       | 7,000          | 11,260         | 8,981.33    | 1,110.171                 |
| Age when diagnosed with lymphoedema    | 31       | 31             | 80             | 53.61       | 10.963                    |
| BMI after lymphoedema diagnosis        | 31       | 16.1           | 36.4           | 26.558      | 5.8310                    |

result of the more aggressive surgery plus the radiation required to treat late-stage disease with nodal involvement.

In contrast, however, Werner et al (1991) and Warmuth et al (1998) did not find any correlation between late-stage breast cancer and lymphoedema. Several health factors have been associated with the development of lymphoedema, including patient age at diagnosis (Armer and Fu, 2005; Kiel and Rademacker, 1996; Werner et al, 1991), body mass index (BMI) greater than 26kg/m<sup>2</sup>, hypertension (Bohler et al, 1992; Kocak and Oregaard, 2000) and a history of infection (Harris et al, 1991).

Complete decongestive therapy (CDT) is the recommended treatment for lymphoedema (Didem et al, 2005; Hamner and Fleming, 2007; Jeffs, 2006; McNeely et al, 2004; Moseley et al, 2007; Szuba et al, 2002; NLN Medical Advisory Committee, 2011).

Other treatment modalities include the use of a pneumatic compression pump (Moseley et al, 2007) and the use of drugs, such as benzopyrenes (Moseley et al, 2007; Piller, 1980). Infection treatment (Harris et al, 1991) and other surgical procedures, such as liposuction and macrosurgical or microsurgical techniques, may also be considered (Campisi, 2004; Ridner and Dietrich, 2008; NLN Medical Advisory Committee, 2011).

## Research methods

A descriptive, retrospective survey was used in this study. The medical records of all breast cancer patients treated at Komfo Anokye Teaching Hospital (KATH) oncology unit

from January 1, 2005 to December 31, 2008 were included in the study (*n*=313).

The breast cancer-related variables were breast cancer diagnosis, stage of breast cancer, breast cancer treatment received and number of lymph nodes removed. Meanwhile, lymphoedema variables were lymphoedema diagnosis, date of lymphoedema diagnosis, signs and symptoms of lymphoedema, location of lymphoedema in the arm, BMI and lymphoedema treatment.

Additional data collected included date of first registration, year treatment began, gender and age.

## Data analysis

The collected data were analysed as descriptive statistics using SPSS software version 17.0. Descriptive statistic techniques were applied to variables such as age, BMI prior to lymphoedema, systolic and diastolic blood pressure, radiation dose, BMI during lymphoedema, as well as age in years when diagnosed with lymphoedema.

Frequency tables were used in the data analysis for variables such as the year the patient started receiving treatment at KATH, gender, marital status, the treatment received at KATH, the location of lymphoedema in the arm and the signs and symptoms associated with lymphoedema. The percentages, mean, minimum and maximum values of these variables were calculated.

## Study findings

### Age

Of 313 medical records reviewed, the youngest age was 22 and the oldest age was 95 years of age. The mean age of this

study was 50.65 years (Standard deviation (SD)=12.232).

### Body mass index prior to lymphoedema

The minimum BMI (*n*=305) was 13.2kg/m<sup>2</sup> and the maximum body mass index was 65kg/m<sup>2</sup>. The mean body mass index was 25.699kg/m<sup>2</sup> (SD=6.0129 kg/m<sup>2</sup>).

### Systolic blood pressure

The minimum and maximum systolic blood pressure measurements (*n*=309) were 80mmHg and 180mmHg respectively with 130.56 as the mean (Standard deviation: Std=16.588) mmHg (Table 1).

### Diastolic blood pressure

The minimum and maximum diastolic blood pressure measurements (*n*=309) were 50 mmHg and 120mmHg respectively, with 81.73 mmHg as the mean (SD=10.463 mmHg).

### Radiation dose

Fifty-seven per cent of the patients (177 out of 313) received radiation treatment. The minimum radiation dose was 48 Centigray (cGray) and 13512 cGray was the maximum dose. The mean was 8935.12 cGray with a standard deviation: Std=1969.519 cGray.

### Treatments for breast cancer

Mastectomy was performed on 123 (39.2%) breast cancer patients. The majority (60.7%; (*n*=190) did not have a mastectomy. The number of breast cancer patients that underwent lumpectomy was 87 (27.8%). Lumpectomy was not performed on the majority, 72.2% (*n*=226) of the patients.

Table 2 shows that only 20.4% ( $n=64$ ) of the patients had axillary lymph node dissection. The majority of the patients, 79.6% ( $n=249$ ) did not undergo axillary lymph node dissection. Only two of the 313 (0.6%) patients had sentinel lymph node biopsy (Table 3). The number of breast cancer patients who received radiation treatment was 117 (56.5%) while 136 (43.5%) did not (Table 4).

### Lymphoedema patients

The number of patients who developed lymphoedema after treatment was 31 (9.9%). The majority of the patients, 282 (90.1%) did not develop lymphoedema after treatment.

The mean time of onset of lymphoedema was 9.7 months, the median was 10.2 months ( $SD=7.5$  months). The maximum time of onset of lymphoedema was 25.4 months.

The majority of the lymphoedema patients, 64.5% ( $n=20$ ) had late-stage breast cancer disease (stage four) followed by 12.9% (stage four) with stage two and 9.7% (stage three) also with stage three breast cancer. Only 3.2% of the lymphoedema patients had stage one breast cancer disease. For the remaining 6.5% (stage two) of the lymphoedema patients, their breast cancer stages were either unknown or not stated in the patient medical records.

The majority of the lymphoedema patients, 77.4% ( $n=24$ ) did not have hypertension. Only seven out of 31 lymphoedema patients (22.6%) were hypertensive.

As shown in Table 4, there are variations in all factors analysed for the 31 cases of lymphoedema. Also note that only 21 of the lymphoedema cases received radiation as part of their treatment.

The number of lymphoedema patients that underwent axillary lymph node dissection was 38.7% ( $n=12$ ). The majority, 61.3% ( $n=19$ ) of the lymphoedema patients did not undergo axillary lymph node dissection.

In Table 5, the cross tabulation of patients who underwent axillary lymph node dissection and developed lymphoedema and the patients who did not develop lymphoedema is shown. Sixty-four of the 313 patients had axillary lymph node dissection of which 12 developed lymphoedema and 52 did not develop lymphoedema.

The chi-square test shows a significant relationship between having had axillary lymph node dissection and being diagnosed

**Table 2.** Axillary lymph node dissection.

| $n=313$                        |           |                |                     |
|--------------------------------|-----------|----------------|---------------------|
| Axillary lymph node dissection | Frequency | Valid per cent | Cumulative per cent |
| Yes                            | 64        | 20.4           | 20.4                |
| No                             | 249       | 79.6           | 100.0               |
| Total                          | 313       | 100.0          |                     |

**Table 3.** Sentinel lymph node biopsy.

| $n=313$                    |           |                |                     |
|----------------------------|-----------|----------------|---------------------|
| Sentinel lymph node biopsy | Frequency | Valid per cent | Cumulative per cent |
| Yes                        | 2         | 0.6            | 0.6                 |
| No                         | 311       | 99.4           | 100.0               |
| Total                      | 313       | 100.0          |                     |

**Table 4.** Radiation.

| $n=313$   |           |                |                     |
|-----------|-----------|----------------|---------------------|
| Radiation | Frequency | Valid per cent | Cumulative per cent |
| Yes       | 177       | 56.5           | 56.5                |
| No        | 136       | 43.5           | 100.0               |
| Total     | 313       | 100.0          |                     |

with lymphoedema (Chi-square test value=7.055,  $P=0.008$ ).

## Discussion

### The incidence of lymphoedema

In this descriptive retrospective survey on the medical records of all the 313 breast cancer patients treated at KATH between January 1, 2005 and December 31, 2008, 31 (9.9%) developed lymphoedema. Despite the relatively low incidence of lymphoedema found in this study, it falls within the reported range of 5% to 60% in the literature (Loudon and Petrek, 2000; Clark, et al, 2005; Sakorafas et al, 2006; Poage et al, 2008).

### Time of onset of lymphoedema in this study

Several studies (Loudon and Petrek, 2000; Clark et al, 2005; Sakorafas, et al, 2006; Poage et al, 2008) show that lymphoedema can occur at any time after breast cancer treatment. In this study, lymphoedema onset ranged from immediately after treatment (0 month) to 25 months after treatment, with 10 months as the median.

### Risk factors of lymphoedema in this study

The literature identifies the following risk factors associated with lymphoedema: axillary lymph node dissection, radiation, the stage of breast cancer diagnosis, high body mass index, age and hypertension.

This study found that axillary lymph node dissection is a statistically significant risk factor associated with lymphoedema (Chi-square test value=7.055,  $P=0.008$ ).

The findings of this study are consistent with previous studies that identified axillary lymph node dissection as a significant risk for lymphoedema (Blanchard and Donohue, 2003; Golshan and Martin, 2003; Schijven et al, 2003). The performance of a mastectomy and lumpectomy without axillary lymph node dissection was not found to be significantly associated with lymphoedema in this study, as was found in a study by Meric et al (2002).

Previous studies have identified radiation to be a significant risk factor associated with arm lymphoedema, especially when the radiation dose is greater than 5000 cGray (Hinrichs, et al, 2004; Yao, 2004; Hanks, et al, 2006; Bani et al, 2007).

**Table 5.** The cross tabulation of axillary lymph node dissection and patients with or without lymphoedema.

|                                       |     |                                         |                            |        | <i>n</i> =313 |
|---------------------------------------|-----|-----------------------------------------|----------------------------|--------|---------------|
| <i>Axillary lymph node dissection</i> |     |                                         | <i>Lymphoedema patient</i> |        | <i>Total</i>  |
|                                       |     |                                         | Yes                        | No     |               |
| Axillary lymph node dissection        | Yes | Count                                   | 12                         | 52     | 64            |
|                                       |     | % within axillary lymph node dissection | 18.8%                      | 81.3%  | 100.0%        |
|                                       | No  | Count                                   | 19                         | 230    | 249           |
|                                       |     | % within axillary lymph node dissection | 7.6%                       | 92.4%  | 100.0%        |
| Total                                 |     | Count                                   | 31                         | 282    | 313           |
|                                       |     | % within Axillary lymph node dissection | 9.9%                       | 90.1%  | 100.0%        |
| BMI after lymphoedema diagnosis       | 31  | 16.1                                    | 36.4                       | 26.558 | 5.8310        |

In this study, of the 31 patients who developed lymphoedema, 21 received a minimum radiation dose of 7000 cGray [1]. However, radiation was not a statistically significant risk factor of lymphoedema in this study but may have contributed to the development of lymphoedema ( $P>0.05$ ).

Late-stage breast cancer with a spread to the lymph nodes results in having more aggressive surgery along with radiation to the axilla, thus increasing the lymphedema risk (Schunemann and Willich, 1997; Park et al, 2008; Swenson et al, 2009).

Although late-stage breast cancer was not found to be a statistically significant risk of lymphoedema ( $P>0.05$ ), in this study the majority (64.5%) of the lymphoedema patients did have late-stage breast cancer.

Age has been reported by many studies as a contributing factor associated with lymphoedema (Werner et al, 1991; Kiel and Rademacker, 1996; Armer and Fu, 2005).

This study provides evidence showing no statistically significant differences in age between those patients who developed lymphoedema and those who did not (all  $P$  values were  $>0.05$ ).

BMI greater than 26kg/m<sup>2</sup> has been found statistically to be a significant risk of arm lymphoedema in breast cancer patients (Werner et al, 1991; Clark et al, 2005; Park et al, 2008). BMI was not found to be a statistically significant risk factor of lymphoedema in this study ( $P>0.05$ ). Even though high BMI in this study was not

significantly associated with lymphoedema (Table 1), the mean BMI of 26.2kgm<sup>2</sup> is high and thus may have contributed to the development lymphoedema.

There is evidence showing that hypertension is another contributing risk factor of developing lymphoedema in breast cancer patients. While two studies demonstrate hypertension as a contributing risk factor in developing lymphoedema (Bohler et al, 1992; Kocak and Oregaard, 2000), the findings of this study show no significant differences in the systolic and diastolic blood pressures between those patients who developed lymphoedema and those who did not ( $P>0.05$ ). Therefore, hypertension was not a statistically significant risk factor of lymphoedema in this study.

### Implications of findings for nursing practice

This study provides evidence that the incidence of lymphoedema following breast cancer treatment was 9.9% with axillary lymph node dissection as the only statistically significant risk factor. Radiation and the stage of breast cancer at diagnosis may have contributed to the development of lymphoedema in this study. High BMI, age and hypertension were not associated with lymphoedema.

With the majority of breast cancer patients not only presenting with the disease at a late stage, but also undergoing axillary

lymph node dissection, lymphoedema will continue to be a problem in Ghana. Knowing the incidence and risk factors of lymphoedema not only helps in the early detection and effective treatment of lymphoedema, but this knowledge also provides the baseline data for future lymphoedema research in Ghana.

### Future research

A long-term prospective study, with a larger sample size, involving other hospitals will be of great value. Additional research using volume measurement in defining the incidence of lymphoedema is needed.

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