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Research Article

Positive Tumor Margins in Wide Local Excision of Breast Cancer: A 10-Year Retrospective Study

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Abstract *Background.* The safety of wide local excision as a standard surgical option for early stage breast cancer management in Ghana has not been evaluated. The aim of this study was to use retrospective histopathological descriptive study to evaluate the prevalence of positive tumor margins in wide local excision specimens and offer recommendations. *Study design.* We reviewed 147 breast lumps, following wide local excision, which were received in the Department of Pathology, for positive tumor margins. The data was analyzed using SPSS software (version 16). *Results.* A total of 2,751 female breast cancers were diagnosed during the study period, of which 147 (5.3%) were from wide local excisions (lumpectomies). Thirty-one (21.0%) had positive tumor margins. The mean age of women with positive margins was 53.4 (SD = 17.1) years. The mean size of primary tumor was 4.0 (SD = 2.1) cm, the majority (53.0%) of which were greater than 2.0 cm, but less than or equal to 5.0 cm (T2). A total of 26 (83.4%) of these tumors were invasive ductal carcinomas (NOS), 24 (92.3%) of the cases had combined Bloom-Richardson grading, and many, 10 (41.7%), were grade 1. *Conclusion.* Our study shows that 21.0% of all wide local excision biopsies had positive tumor margins, a figure that is comparable to those of other studies. Tumors with positive margins in this study were large, 4.0 cm (T2), and common in relatively young women. Treatment failure is therefore likely to occur in these patients.

Keywords early breast cancer; lumpectomy; wide local; positive margins; prevalence

1. Introduction

Lumpectomy is a standard surgical procedure in the management of early stage breast cancer [30]. It is usually preceded by the initial diagnostic workup consisting of clinical and radiological assessment and biopsy for histological confirmation. Surgery is then aimed at securing a widely clear rim of normal tissue surrounding the carcinoma and at the same time leaving behind adequate breast tissue for good cosmetic results. The excised lump is sent for histopathological analysis, which includes assessing all margins for malignant cells (positive margins). There is no consensus as to what constitutes a positive or negative margin [1,4,22], but some studies considered a margin superior or equal to 3.0 mm as negative [23]. The prevalence of positive tumor margins in lumpectomies from published data varies widely, ranging from 4% to 31% [12,17,33,34]. Positive margins are a major risk factor for the development of local recurrence [2,5,7,18,19], and systemic disease [15, 16]. Breast cancer is said to be commoner in young Ghanaian women [9,8,11]. Younger age at diagnosis is found to be a risk factor for positive margins [21,32,35]. Some literature seem to suggest that there is no relationship between size of the primary tumor, histologic grade, nodal involvement, and positive margins [3,6,10,20,31]. Contrary to this view, other studies found tumor size, grade, and nodal involvement to be associated with positive margins and increased risk of local recurrence [13,14,15,24,25,26].

Lumpectomy has been performed in Ghana over the years as a standard management option for the treatment of early breast cancer. To the best of our knowledge there is no study that has evaluated the safety of lumpectomy as a surgical option for the treatment of early breast cancer. However, Der et al. (2013) in their study "Positive malignant margins in clinically diagnosed and excised benign breast lumps" found that 321 (11.0%) out of 2,917 excised breast lumps were malignant and that 142 (44.0%) had positive tumor margins [9]. The aim of this study is to use retrospective histopathological descriptive study to evaluate the prevalence of positive tumor margins among wide local excision (lumpectomy) specimens of Ghanaian women with early breast cancer treated by this method and to suggest some recommendations.

2. Materials and methods

We retrospectively reviewed all wide local excision (lumpectomy) specimens of patients with early breast cancer in our institution over a 10-year period (2002 to 2011), for positive tumor margins. The patient's age, duration of the symptom, and tumor variables (primary

tumor size, histologic type, grade, TNM stage, and presence of positive margins) were reviewed by two specialists. The data was entered into SPSS software (version 18) and analyzed. Results were presented in frequency tables. Associations between tumor variables and positive tumor margins were determined.

In this study, the definition of positive margins was based on the following criteria:

- tumor cells within 2.0 mm of one or more resection margins;
- tumor cells within one or more inked margins;
- tumor extends to one or more resection margins as stated by the pathologist.

All the investigations were done on paraffin-embedded breast cancer tissues.

In this study, histological subtyping of tumors was based on the architecture and cytological features of the tumor, the grading was according to the modified Bloom-Richardson grading system, and the TNM staging (sixth edition) was that used by the American Joint Committee on Cancer (AJCC), that takes into account the size of the primary tumor (T), the number of cancerous lymph nodes (N), and the presence of metastatic disease (M). In this study, not all the lumpectomies had lymph node dissection and, thus, full TNM staging. Also evidence of lympho-vascular invasion was recorded.

Inclusion criteria

Specimens that met any of the three criteria above were recorded as having positive margins.

Exclusion criteria

All simple excision breast specimens and mastectomies were excluded.

3. Results

3.1. Clinical characteristics of the 147 cases

From January 2002 to December 2011, a total of 65,638 surgical specimens were received in our institution, of which 7,214 (11.0%) were breast samples from female patients. Two thousand seven hundred and fifty-one (38.1%) of the breast specimens from female patients were malignant, of which 147 (5.3%) were diagnosed in wide local excisions (lumpectomies). The ages of the women who had lumpectomies as a surgical treatment for early breast cancer ranged from 24 to 98 years, with 48 (32.9%) in the modal age group of 40–49 years. The mean age of the women was 48.1 years (SD = 13.2). The majority, 88 (59.9%), were younger than 50 years of age (see Table 1). The age of one woman was not stated. The commonest 146 (99.3%) clinical presentation was lump in the breast. The duration of the lump at presentation was stated in only 15 (11.0%) of the women who had lumpectomies. Of these, 6 (40.0%), reported within one to three months of noticing the lump. The macroscopic size of primary tumor ranged from 0.7 cm to 13.0 cm (the largest was a malignant phyllodes tumor) with a mean of 3.8 cm (SD = 3.8). Many, 61 (46.2%), were greater than 2.0 cm, but less than or equal to 5.0 cm (T2). Of the 36 (26.3%) who had previous diagnosis more than half, 24 (58.35), were excision biopsies (Table 1).

Table 1: Clinical characteristics of wide local excision biopsies (lumpectomies).

	Frequency (n)	Percentage (%)
Age (years)*		
≤ 39	40	27.4
40–49	48	32.9
50–59	28	19.2
≥ 60	30	20.5
Total	146	100.0
Duration of symptoms (months)#		
1–3	12	28.6
4–6	11	26.2
7–12	15	35.7
> 12	4	9.5
Size of primary tumor (cm)		
≤ 2.0	42	28.6
$> 2 \leq 5$	75	51.0
> 5	30	20.4
Total	147	100.0

*No stated age for one case.
#No stated size of primary tumor in 15 cases.

3.2. Histological characteristics of all cases

A total of 124 (84.4%) of the breast cancers were invasive ductal carcinoma not otherwise specified (NOS), followed by 8 (5.8%) ductal carcinoma in situ (DCIS). Eighty-seven (70.2%) of the NOS were graded by the combined Bloom-Richardson grading and many of them, 36 (41.4%), were grade 2 (Table 2). Of those that had both wide local excision and axillary lymph node dissection, positive nodes ranged from 1 to 11 lymph nodes with a mean of 3.1 lymph nodes (SD = 2.4). A total of 46 (39.3%) of the NOS had TNM staging, of which many, 25 (54.3%), were stage 2. Seven (4.8%) of the tumors showed lymphovascular invasion in this study.

A total of 31 (21.1%) of the cases had positive tumor margins (Table 2).

3.3. Clinico-pathological characteristics of 31 primary tumors with positive margins

The ages of the 31 women with positive tumor margins ranged from 24 years to 98 years, with a mean age of 53.4 (SD = 17.1) years. The mean size of primary tumors in this category was 4.0 (SD = 2.1) cm. Many of the tumors, 16 (53.0%), were greater than 2.0 cm, but less than or equal to 5.0 cm (T2). Majority (84%) of excised tumors with positive

Table 2: Histologic characteristics of lumpectomy specimens.

	Frequency (n)	Percentage (%)
Histologic subtypes of breast cancers		
Invasive ductal (NOS)	124	84.4
Ductal carcinoma in situ (DCIS)	8	5.4
Lobular	4	2.7
Mucinous	3	2.0
Medullary	2	1.4
Others	6	4.1
Total	147	100.0
Histologic grade		
I	20	23.3
II	36	41.9
III	30	34.8
Total	87	100.0
Positive margins	31	21.0

NOS: Invasive ductal carcinoma not otherwise specified.

cancer margins were invasive ductal carcinomas (NOS), 24 (92.3%) of which had combined Bloom-Richardson grading, most of them, 10 (41.7%), being grade 1 (Table 3).

3.4. Associations between size of primary tumor with positive tumor margins and the other tumor variables

Using spearman's correlation, we found a significant association (P-value $= 0.009$) between size of primary tumor and the grade of the tumor. We did not find significant association between the size of primary tumor and the following parameters: age at diagnosis, histologic type, TNM stage, and positive lymph nodes (Table 4).

4. Discussion

The goal of breast conservation surgery (BCS) is to completely remove the identified cancer while preserving adequate breast tissue to achieve an acceptable cosmetic result. The presence of a microscopically clear surgical margin is the most important indicator of completeness of surgical excision. During the ten-year scope of our review, 31 (21.1%) of all wide local excision biopsies had positive tumor margins. Published rates of positive margins in lumpectomies vary widely, ranging from 4% to 31% [12, 17,33,34]. Our rate of 21.1% is in accord with these studies. However, this value is lower than Der et al. studies of positive malignant margins in clinically diagnosed and excised benign breast lumps, in which they found that 322 (11.0%) out of 2,917 clinically benign lumps during the study period were malignant and that 142 (44.1%) had positive margins [9]. The high rate of positive margin in that study was because the excisions were not wide local excisions. Various studies have shown that positive margins are a major risk factor for the development of local recurrence [2,5,7,18,19] and systemic disease [15,16]. The presence of positive margins generally leads to further surgical resections, with associated morbidity, resource utilization, anxiety, and delay in seeking care.

Table 3: Clinico-pathological characteristics of biopsies with positive margins.

	Frequency (n)	Percentage (%)
Age (years)		
≤ 39	7	22.6
40–49	9	29.0
50–59	6	19.4
≥ 60	9	29.0
Total	31	100.0
Size of primary tumor (cm)		
2.0	6	19.4
$> 2 \leq 5$	20	64.5
> 5	5	16.0
Total	31	100.0
Histologic subtypes		
Invasive ductal (NOS)	26	83.9
Ductal carcinoma in situ (DCIS)	2	6.5
Mucinous	2	6.5
Medullary	1	3.2
Total	31	100.0
Histologic grade		
I	10	41.7
II	6	25.0
III	8	33.3
Total	24	100.0

In our study, the mean age of women with positive margins was 53.4 years, with a modal age group of 40–49 years. This age group is similar to the findings in previous studies in Ghana [9,8,11]. Young age has generally been found to be associated with an increased risk of local recurrence after breast conserving surgery [21,32,35]. There is no exact reason for the increased risk in this age group, but Maurice et al. argued that a possible explanation for the recurrence is the occurrence of new primary tumor [32]. The mean size of specimens with positive margins was large, 4.0 cm with many (51.0%) been T2. We found significant association ($P = .009$) between tumor size and grade of the tumors. We did not find significant association between size of primary tumor and age at diagnosis, histological type, TNM stage, and positive lymph nodes. This finding is similar to some published literature that did not find significant positive association between the size of primary tumors with positive margins and the other tumor variables [10,20,31]. This, however, differs *from* some other studies *on* breast conserving surgery *that* found strong association between size of primary tumors with positive margins and other tumor variables, particularly where the pathological tumor size was greater than 2 cm, and hence a predictor of local recurrence [3,6,13,14,15,24, 25,26]. Aside these traditional risk factors that are known to be associated with positive tumor margins, the size ratio tumor/volume of the breast and patient's consent are other

Table 4: Associations between the size of primary tumors with positive margins and the other tumor variables.

	Age (years)	Histology subtype	Histologic grade	Tumor size (cm)	Positive lymph node
Age (years)	—	0.863	0.648	0.962	0.840
Histology subtype	0.863	—	—	0.243	0.217
Histologic grade	0.648	—	—	0.009	0.744
Tumor size (cm)	0.962	0.243	0.009	—	0.588
Positive lymph node	0.840	0.217	0.744	0.588	—

factors that can increase the incidence of positive margins in excised cancerous breast lumps [27, 28, 29]. For instance, a breast that contain cancer may affect the surgeon ability to secure cancer free margins. Similarly for cosmetic reasons or those refusing systematically mastectomy the amount of breast tissue to be excised may be limited [27, 28].

5. Conclusion

Our study shows that 21.0% of all lumpectomies have positive tumor margins, a figure that is comparable to those of other studies. Tumors with positive margins in this study were large, 4.0 cm (T2), and common in relatively young women. Treatment failure is therefore likely to occur in these patients.

Recommendations The margins of all wide local excision specimens should be assessed for positive margins in order to identify those at risk of developing local recurrence. Frozen section technique should be instituted to help the surgeon achieve negative margins intraoperatively.

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