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Cording Following Treatment for Breast Cancer

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Abstract

Background—Treatment for breast cancer may result in the formation of palpable cords in the axillary region. Our aim was to evaluate cording incidence, risk factors, and association with upper extremity functional impairment and measured arm volume change.

Methods—We included 308 patients with unilateral breast cancer prospectively screened for upper extremity lymphedema, symptoms and function. Patients were assessed pre- and post-operatively and at 3 – 8 month intervals with perometer arm measurements and the LEFT-BC questionnaire. Cording was determined by patient self-report. The cumulative incidence of cording and its association with clinicopathologic factors, upper extremity functional impairment, and measured arm volume change were analyzed.

Results—31.5% (97/308) of patients reported cording, with a cumulative incidence of 36.2% at 24 months post-operative. Clinicopathologic factors significantly associated with cording by multivariate analysis included axillary lymph node dissection ($p < .0001$) and younger age at diagnosis ($p = 0.0005$). Cording was associated with increased functional impairment ($p = 0.0018$) and an arm volume increase of 5% ($p = 0.028$).

Conclusions—Cording following breast cancer treatment is common, and may occur beyond the post-operative period. Our findings emphasize the importance of identifying patients at high risk for cording, and developing strategies to minimize functional impairment and arm volume elevation associated with cording. Future studies should investigate the effectiveness of interventions for cording following breast cancer treatment.

INTRODUCTION

Cording, also known as axillary web syndrome (AWS), is a condition which may develop as a result of breast cancer treatment. Cords are palpable bands of tissue which can occur in the axilla, across the antecubital fossa into the forearm and wrist, and in the breast or abdominal wall[1–3]. The incidence of cording following breast cancer treatment ranges from 6 – 72%[3–5], and the condition can cause pain and limited range of motion in the upper

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extremity[1, 4–8]. Cording is reported to occur in the early post-operative period, and resolve within three months of surgery[2–4, 6].

The etiology of cording is not fully understood. The condition may be related to abnormalities in either the axillary vasculature or the lymphatics[2,3,9]. Anatomic studies of resected cords reveal that these structures may represent dilated and thrombosed lymphatics and/or thrombosed superficial veins[3,9]. The condition is considered to be a variation of Mondor's disease, a rare thrombophlebitis of the subcutaneous veins caused by trauma such as surgery[10].

The incidence of cording after axillary lymph node dissection (ALND) has been reported as high as 72%, compared to 20% after sentinel lymph node biopsy (SLNB)[4]. Younger age, lower BMI, and being African-American have also been implicated as potential risk factors[1, 11]. While cording has been reported to cause limited range of motion, the extent to which this translates into dysfunction performing daily functional reaching activities has yet to be reported. In addition, little data exists on whether cording is associated with an increased risk of developing upper extremity lymphedema.

We sought to determine the incidence of cording in a prospective cohort of women treated for breast cancer. We evaluated clinicopathologic risks factors for cording, and analyzed the association of cording with upper extremity functional impairment and measured arm volume change.

METHODS

Study Design and Patients

Women diagnosed with primary breast cancer are offered enrollment into a lymphedema screening trial at the time of pre-operative consult at our institution. This trial is approved by the Institutional Review Board [Clinical Trials.gov Identification number NCT01521741], and the primary aim is early lymphedema detection through prospective arm volume measurements with a perometer. A secondary aim is to assess upper extremity symptoms and function using the Lymphedema Evaluation Following the Treatment for Breast Cancer (LEFT-BC) Questionnaire, which contains sections from validated surveys including the Lymphedema Breast Cancer Questionnaire (LBCQ)[12], the Disability of the Arm Hand and Shoulder (DASH)[13], and a limited number of questions designed by our study team.

Per protocol, patients are assessed pre- and post-operatively, and every 3–8 months with perometer arm measurements and the LEFT-BC Questionnaire. As previously published, arm volume change is quantified using the Relative Volume Change (RVC) equation, $RVC = (A(2)U(1)/U(2)A(1)) - 1$ where A(1) and A(2) are arm volumes on the side treated for breast cancer at the pre-operative assessment and a follow-up assessment, and U(1) and U(2) are arm volumes on the untreated side at the corresponding time points[14].

Patients included in this analysis were enrolled between 8/2009 – 5/2012, underwent unilateral breast surgery at our institution, had a pre-operative assessment, a postoperative assessment (3 months after surgery), and at least one follow-up assessment occurring > 3 months after surgery. Patients with bilateral breast or axillary surgery, distant metastasis or recurrence were excluded.

Assessment for Cording

Cording was determined by self-report via the LEFT-BC Questionnaire, which contains the following explanation: “As your body heals following treatment for breast cancer, sometimes bands of tissue can form in your armpit or down your arm that look like strings

or thin ropes. This is called **cording**.” The questionnaire also has an image of cording to aid patients in identifying the condition (Figure 1).

Patients were asked to indicate if, during the past month, they “saw or felt a thin cord or string in any of the following areas: in your armpit that extends into the inside of your upper arm, across the inside of your elbow, along your forearm and wrist, under your breast extending toward your abdomen, or none of the above.” Patients were classified as having cording if they responded “yes” to any of the above locations.

Validation of Self-Report for Cording Assessment

To determine the validity of self-report for cording assessment, a subset of patients who reported cording were examined by trained research coordinators for visible cording. Patients who reported cording which was not visible were referred for clinical examination by a nurse practitioner to see if cording could be palpated. Patients who reported cording only under the breast were not examined due to restrictions by the IRB. Between 9/2012 and 1/2013, 47 of 443 consecutive patients on the screening trial reported cording. 3 of the 47 patients indicated cording only under the breast and were therefore not examined. Of the remaining 44 patients, 41 (93%) had visible cording, and 2 (5%) had cording which was not visible but was confirmed by clinical exam. One patient did not have visible cording and did not undergo an exam due to the lack of an available nurse practitioner. Therefore there was a maximum of 4 false positives for cording (including the 3 patients with cording under the breast only), resulting in 91.5% specificity (95% CI: 79.6% – 97.6%) of self-report for cording assessment.

Clinicopathologic Factors

Data on patient demographics and breast cancer treatment was collected via medical record review and analyzed for association with cording. Hand dominance was collected at the pre-operative assessment.

Measured Arm Volume

We examined cording as a risk factor for a measured arm volume increase of 5% RVC, occurring on the same date or after cording was reported. Measurements 3 months post-operative were not utilized in order to exclude cases of post-operative swelling.

Upper Extremity Functional Impairment

To evaluate upper extremity functional impairment, we analyzed questions pertaining to functional reaching activities from the LEFT-BC Questionnaire. Patients were asked to rate how easily the following activities could be performed on a scale from 1 – 5 (1 = easily, 2 = some difficulty, 3 = great difficulty, 4 = unable to do, 5 = never attempted):

- place something on a shelf above head
- pull a tight shirt on over my head
- push open a heavy door
- clean a window above shoulder height
- catch a falling object with affected hand

A functional impairment score corresponding to each assessment was calculated by averaging the patient’s ratings for the above activities, with higher score indicating greater impairment. The “never attempted” rating was excluded. Average percent (%) change in functional impairment score compared to pre-operative was calculated to account for pre-

existing functional impairment. Cording and other clinicopathologic factors were analyzed as risk factors for average % change in functional impairment score.

Statistical Analysis

Cumulative incidence of cording was estimated using actuarial (Kaplan-Meier) analysis. Univariate and multivariate Cox proportional hazards models were used to analyze risk factors for cording and arm volume change. Time-dependent covariates were used when appropriate for risk factors that develop during follow-up, such as RVC 5% (in the cording analysis) and cording (in the arm volume change analysis). Linear models were used to assess predictors of upper extremity functional impairment.

RESULTS

Study Population and Cording Incidence

1175 patients were offered enrollment into the lymphedema screening trial at their pre-operative assessment between 08/2009 – 05/2012, of which 838 (71%) agreed to participate. 530 patients agreed to participate but were excluded, 142 for bilateral surgery and 388 due to 1) treatment at another institution, 2) lack of adequate follow-up at the time of analysis, or 3) removal after enrollment due to not meeting study criteria. Therefore 308 patients met inclusion criteria. Clinicopathologic characteristics are listed in Table 1. Median post-operative follow-up was 15.8 months (range 4.2 – 38.9), with a median of 5 assessments per patient (range 3 – 21). The median time from surgery to the first assessment was 0.8 months (range 0.2 – 3.1).

97 of 308 (31.5%) patients reported cording, of which 51.5% (50/97) first reported cording 3 months post-operative (Figure 2). Median time to first report of cording was 2.5 months post-operative (range 0.6 – 24.0). The cumulative incidence of cording was 16.2% at 3 months (95% CI: 12.6% – 20.6%), 23.4% at 6 months (95% CI: 19.0% – 28.5%), 29.2% at 12 months (95% CI: 24.3% – 34.7%), and 36.2% (95% CI: 29.9% – 43.2%) at 24 months post-operative (Figure 3).

Of the 97 patients with cording, 68 (70%) reported cording in the armpit extending into the inside of the upper arm only, 7 (7%) across the inside of the elbow, 7 (7%) along the forearm and wrist, and 12 (12%) under the breast extending toward the abdomen only. 3 (3%) patients did not report the location of the cord.

Cording Risk Factors

Univariate values for association of clinicopathologic factors with cording are listed in Table 1. The median post-operative follow-up was 19.3 months for patients who reported cording, and 14.9 months for those without cording. By multivariate analysis, only ALND ($p < .0001$) and younger age at diagnosis ($p = 0.0005$) were significant risk factors for cording (Table 2).

Patients who first reported cording >3 months post-operative ($n=47$) did not significantly differ from those who first reported cording 3 months after surgery ($n=50$) in age or BMI at diagnosis, type of breast or axillary surgery, average pre-operative functional impairment score, or neoadjuvant chemotherapy status ($p > 0.05$ for all).

Upper Extremity Functional Impairment

By univariate analysis, average % change in functional impairment score from pre-operative was significantly greater for patients with cording (mean = 32%) compared to those without cording (mean = 15%, $p < .0001$, Figure 4). By multivariate analysis, factors significantly associated with increased average % change in functional impairment score included

cording ($p=0.0018$), mastectomy ($p<.0001$), and ALND ($p=0.0007$). Age and BMI at diagnosis, hand dominance, and arm volume change (maximum RVC of 5%) were not significant ($p>0.05$).

Of the 97 patients with cording, 46 (47%) had a maximum % change in functional impairment score at an assessment prior to first report of cording, 30 (31%) at the same assessment, and 21 (22%) at an assessment after cording was first reported.

Measured Arm Volume Change (RVC $\geq 5\%$)

16.2% (50/308) of patients had an arm volume increase of 5% RVC, which occurred at a median of 7.2 months post-operative (range 3.1–32.3). By multivariate analysis, cording (HR: 1.8, 95% CI: 1.1–2.9, $p=0.028$), ALND (HR: 2.0, 95% CI: 1.2–3.4, $p=0.0078$), and hand dominance on the contralateral side (HR: 1.7, 95% CI: 1.0–2.7, $p=0.036$) were significantly associated with an arm volume increase of 5% RVC. Age and BMI at diagnosis, breast surgery, SLNB, and maximum increase in functional impairment score were not significant ($p>0.05$).

DISCUSSION

In our prospective study of 308 breast cancer patients, 31.5% (97/308) reported cording, with a cumulative incidence of 36.2% at 24 months. Independent risk factors included ALND and younger age at diagnosis, and cording was associated with upper extremity functional impairment and elevated arm volume. Our data suggests that cording is common and may occur beyond the post-operative period. Clinicians and patients should be educated about the risk factors for cording, and aim to develop preventative and intervention strategies to minimize upper extremity functional impairment and arm volume elevation associated with cording.

The incidence of cording following breast cancer treatment is reported to range from 6 – 72%[3,4]. In our series, 31.5% of patients developed cording, with approximately half occurring in the early post-operative period which is consistent with previous reports[1,3,4]. In contrast with other studies, patients in our series remained at risk for cording as late as 24 months following surgery. The late onset of cording has rarely been reported except for two previous studies with more than 3 months of follow-up, which similarly noted that patients could develop cording at later time points [5,6]. Our findings suggest that the late onset of this condition may be underreported.

Consistent with previous reports, we found that ALND was an independent risk factor for cording, but not SLNB[1,3,4,6]. Cording was reported by 54% of patients who underwent ALND, compared to 27% who underwent SLNB. Similarly, Torres Lacombe et al reported a 48% incidence of cording following ALND[6]. The highest incidence was reported by Leidenius et al, who utilized clinical examination of the axilla and arm, and reported a 72% cording incidence following ALND[4]. Of note, 4 patients in our cohort without nodal evaluation reported cording, suggesting that axillary surgery may not be the only contributing factor in cording development.

In addition to ALND, in our series younger age at diagnosis was also an independent risk factor for cording. This may result from younger women being more likely to notice and report cording. However, a similar finding was reported by Bergmann et al, who conducted a physical assessment for cording on breast cancer patients within 45 days of surgery[1]. Others have reported lower BMI to be associated with cording, possibly due to improved ability to detect cording with less axillary subcutaneous tissue[4]. It should be noted that

despite our use of self-report for cording assessment, BMI was not found to be associated with cording in our series.

Due to lack of long-term follow-up, prior studies have not investigated the association of cording with other treatment-related factors such as chemotherapy, radiation, or hormonal therapy. Adjuvant chemotherapy and nodal radiation were significantly associated with cording by univariate analysis, but neither remained significant on multivariate analysis. This likely results from the association of these factors with having undergone ALND, which was found to be the most significant independent predictor of cording in our cohort (HR=2.8). Interestingly, although nodal radiation can cause trauma to the axillary lymphatic vessels and is sometimes reported as a risk factor for lymphedema [15–17], nodal radiation was not found to be an independent predictor of cording in this series.

Reduced range of motion (ROM) of the upper extremity in patients with cording has been previously reported [1,3]. We sought to determine whether these limitations in ROM translated into dysfunction performing daily reaching activities. In our series, cording, in addition to mastectomy and ALND, was associated with increased upper extremity functional impairment. It remains unclear if patients with functional impairment are at a higher risk for cording, or if cording causes an increase in functional impairment. Nearly half of patients in this cohort who developed cording reported a maximum increase in functional impairment prior to the first report of cording. Future research should aim to determine whether early intervention with physical therapy can prevent both functional impairment and cording.

Prior studies have not reported a clear association of cording with the development of upper extremity lymphedema[1,3]. Lymphedema is commonly defined as an arm volume increase of 10%, however, others have suggested that volume increases in the range of 3–5% represent low-level edema[18,19]. The number of events of 10% RVC in our series was low, therefore we utilized 5% RVC to analyze the association of cording with arm volume elevation. Our results demonstrated that cording was an independent risk factor for an arm volume increase of 5% RVC. This suggests that cording may be a risk factor for lymphedema, perhaps because both conditions are lymphatic in origin and result from trauma of the axillary lymphatic system. If future studies demonstrate that cording increases the risk of developing lymphedema, we suggest that patients with cording undergo close screening for lymphedema given reports emphasizing the importance of early detection and intervention for optimal management of the condition[19–24].

Cording is commonly reported as self-limiting, however, interventions including range of motion exercises, non-steroidal medications and heat compressive therapy have been suggested[25]. A retrospective chart review by Wyrick et al and several case studies have suggested the potential benefit of physical therapy for cording resolution[26–29]. Although we did not evaluate treatment for cording in this series, we plan to enroll patients diagnosed with cording into an intervention trial to elucidate the potential benefit of treatment options.

A limitation of our study is assessment for cording primarily by self-report. Our 24-month cumulative incidence of 36.2% is on the higher end compared to previous reports, however, studies utilizing physical exam have reported even higher rates[4]. Additionally, our validation study demonstrated a high specificity of self-report for cording assessment, suggesting that there were few false positives in our cohort. Because patients were assessed every 3–8 months, we were unable to accurately evaluate the duration of cording for patients in this series. Other limitations include too few events of 10% RVC to evaluate cording as a risk factor for lymphedema, and lack of information on whether patients received

interventions for cording. Finally, the median post-operative follow-up for patients with cording was 4.3 months longer than for those without cording.

In conclusion, our data suggests that cording may occur in over 30% of patients treated for breast cancer, and can develop beyond the post-operative period. Patients at risk for cording should be educated about the condition and its association with functional impairment and increased arm volume. Effective preventative and treatment strategies for cording and its associated complications are necessary to maximize short- and long-term quality of life for breast cancer survivors.

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SYNOPSIS

Cording may occur in >30% of patients undergoing treatment for breast cancer, and can develop beyond the post-operative period. Cording is associated with impaired upper extremity function and elevated arm volume, with independent risk factors including axillary lymph node dissection and younger age at diagnosis.



Figure 1.
Image of a cord included in the LEFT-BC Questionnaire

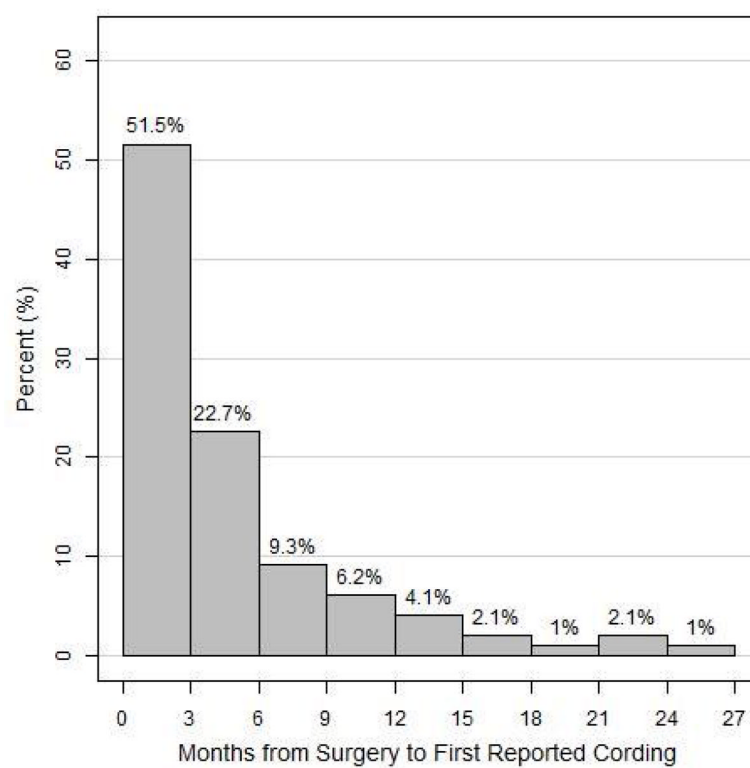


Figure 2.
Histogram of time from surgery to first report of cording

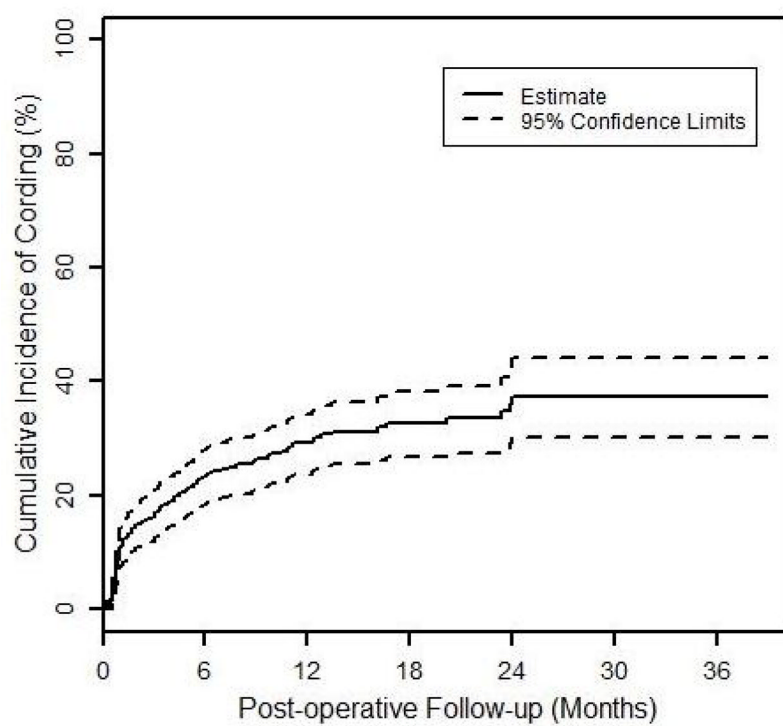


Figure 3.
Cumulative incidence of cording

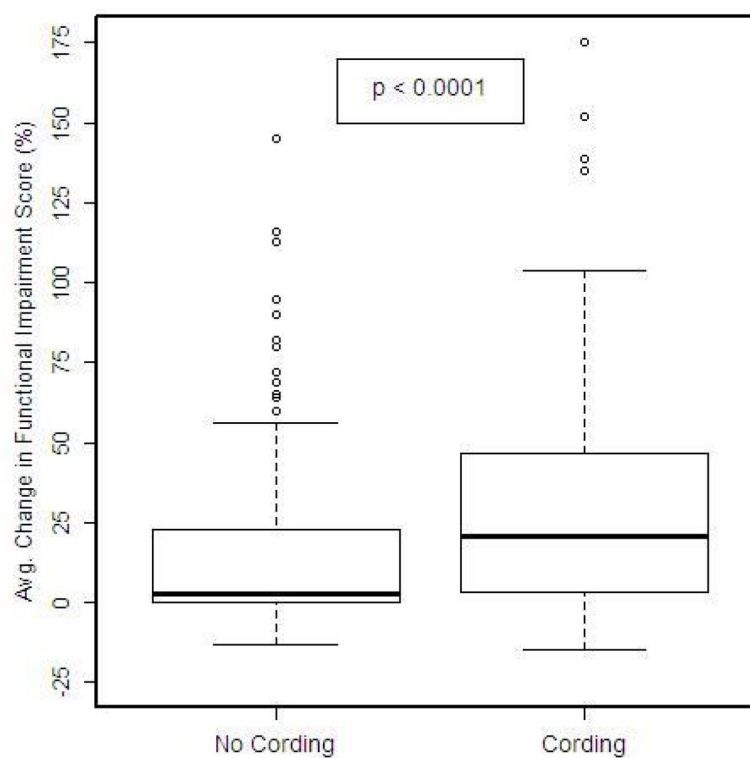


Figure 4.
Change in functional impairment score from pre-operative for patients with and without cording

Table 1

Clinicopathologic characteristics of the study cohort

| | Total Cohort (308 = 100%) | | | | Cording (97 = 31%) | | No Cording (211 = 69%) | | P value |
|--------------------------------------------|---------------------------|---------|----|---------|--------------------|---------|------------------------|--------|---------|
| Patient Characteristics | | | | | | | | | |
| Median age at diagnosis, years | 54 | 32 – 81 | 51 | 32 – 81 | 58 | 37 – 79 | | 0.0004 | |
| Median BMI at diagnosis, kg/m ² | 26 | 17 – 59 | 25 | 19 – 59 | 27 | 17 – 56 | | 0.066 | |
| Hand Dominance | | | | | | | | | |
| | | | | | | | | 0.25 | |
| Ipsilateral Side | 158 | 51% | 44 | 45% | 114 | 54% | | | |
| Contralateral Side | 148 | 48% | 51 | 53% | 97 | 46% | | | |
| Unknown | 2 | 1% | 2 | 2% | - | - | | | |
| Breast Surgery | | | | | | | | | |
| | | | | | | | | 0.044 | |
| Lumpectomy | 234 | 76% | 66 | 68% | 168 | 80% | | | |
| Mastectomy | 74 | 24% | 31 | 32% | 43 | 20% | | | |
| Axillary Surgery | | | | | | | | | |
| | | | | | | | | | |
| None | 30 | 10% | 4 | 4% | 26 | 12% | | - | |
| SLNB | 210 | 68% | 56 | 58% | 154 | 73% | | 0.19 | |
| ALND | 68 | 22% | 37 | 38% | 31 | 15% | | <.0001 | |
| Median # LN's Removed | 2 | 0 – 33 | 3 | 0 – 33 | 2 | 0 – 33 | | <.0001 | |
| Median # Positive LN's | 0 | 0 – 25 | 0 | 0 – 11 | 0 | 0 – 25 | | 0.48 | |
| Neoadjuvant Chemotherapy | | | | | | | | | |
| | | | | | | | | 0.30 | |
| Yes | 24 | 8% | 10 | 10% | 14 | 7% | | | |
| No | 284 | 92% | 87 | 90% | 197 | 93% | | | |
| Adjuvant Chemotherapy | | | | | | | | | |
| | | | | | | | | 0.0093 | |
| Yes | 107 | 35% | 44 | 45% | 63 | 30% | | | |
| No | 201 | 65% | 53 | 55% | 148 | 70% | | | |

| | Total Cohort (308 = 100%) | | Cording (97 = 31%) | | No Cording (211 = 69%) | | P value |
|------------------------------------|---------------------------|-----|--------------------|-----|------------------------|-----|---------|
| | | | | | | | |
| Radiation Therapy | | | | | | | |
| None | 43 | 14% | 12 | 12% | 31 | 15% | - |
| Breast/Chest Wall only | 194 | 64% | 51 | 53% | 145 | 69% | 0.0059 |
| Breast/Chest Wall +nodal radiation | 69 | 22% | 34 | 35% | 35 | 17% | 0.005 |
| | | | | | | | |
| Hormonal Therapy | | | | | | | |
| Yes | 250 | 81% | 79 | 81% | 171 | 81% | |
| No | 58 | 19% | 18 | 19% | 40 | 19% | |

* P-value from univariate Cox proportional hazards model for risk of cording

Reference Group = None

Reference Group = SLNB

Reference Group = None

Reference Group = Breast / Chest Wall Only

* Age, BMI, # LN's Removed, # Positive LN's analyzed as continuous variables

Abbreviations: BMI = Body Mass Index, SLNB = Sentinel Lymph Node Biopsy, ALND = Axillary Lymph Node Dissection, LN = Lymph Node

Table 2

Multivariate analysis of risk factors for cording

| | Hazard Ratio | Lower 95% CI | Upper 95% CI | P value |
|------------------|--------------|--------------|--------------|---------|
| ALND | 2.8 | 1.8 | 4.2 | <.0001 |
| Age at diagnosis | 0.96 | 0.94 | 0.98 | 0.0005 |

Abbreviations: CI= Confidence Interval, ALND= Axillary Lymph Node Dissection