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ORIGINAL ARTICLE

Prevalence and risk factors of adhesive capsulitis of the shoulder after breast cancer treatment

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Abstract
Purpose The present study investigated the prevalence and risk factors of adhesive capsulitis of the shoulder in breast cancer patients between 13 and 18 months after surgery.
Methods This study included 271 women who underwent surgery for breast cancer with a postoperative period of 13–18 months. Current adhesive capsulitis was defined as restriction of external rotation and one or more additional directional restrictions with history of shoulder pain. Cumulative adhesive capsulitis was defined as current adhesive capsulitis or a previous history of adhesive capsulitis after breast cancer surgery. Multivariate logistic regression analysis was performed to examine associations between current or cumulative adhesive capsulitis and potential risk factors.
Results Among the 271 study patients, 28 (10.3%) and 21 (7.7%) had cumulative or current adhesive capsulitis, respectively. The incidences of cumulative and current adhesive capsulitis were higher in those aged 50–59 years (odds ratio [OR], 9.912; 95% confidence interval [CI], 1.790–54.880; and OR, 12.395; 95% CI, 1.187–129.444, respectively) and those who underwent mastectomy (OR, 6.805; 95% CI, 1.800–25.733; and OR, 9.645; 95% CI, 2.075–44.829, respectively) or mastectomy with reconstruction (OR, 13.122; 95% CI, 2.488–69.218; and OR, 20.075; 95% CI, 2.873–140.261, respectively).
Conclusions Adhesive capsulitis of the shoulder is a common problem after breast cancer treatment. An age of 50–59 years and mastectomy are major risk factors for adhesive capsulitis, and breast reconstruction additionally increases the risk. Patients with these risk factors require greater attention for early diagnosis and proper treatment.

Keywords Adhesive capsulitis · Breast cancer · Mastectomy · Shoulder pain · Risk factor

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Introduction

Upper extremity morbidities are common after breast cancer treatment [1]. These can persist for a long time, causing upper extremity impairments and reducing quality of life [2]. Restricted range of motion (ROM) in the shoulder joint is one of the main symptoms of upper extremity morbidities and is associated with reduced quality of life [3]. A study reported 60% of breast cancer patients show reduced shoulder flexion and abduction at 1 month after surgery and 10% of survivors show a persistent ROM reduction at 12 months [4]. Shoulder ROM restriction can be caused by various conditions, such as adhesive capsulitis, pectoralis tightness, and radiation fibrosis.

Adhesive capsulitis, also called frozen shoulder, is a common condition showing insidious onset shoulder pain and global ROM restriction [5, 6]. It has several distinct characteristics from other causes of shoulder ROM restriction after breast cancer treatment. Typically, there is pronounced restriction of external rotation, with multidirectional limitation of motion [7]. Synovial inflammation and subsequent capsular

fibrosis are the underlying pathological changes [8]. Its exact diagnosis and early treatment help to reduce pain and increase the ROM of the shoulder. Therefore, investigation of the risk factors of adhesive capsulitis in breast cancer patients would be helpful for patient education and early treatment. However, there have been few studies on the prevalence and risk factors of adhesive capsulitis in breast cancer patients. Accordingly, the purpose of our current study was to investigate the prevalence and risk factors of adhesive capsulitis in breast cancer patients between 13 and 18 months after surgery.

Methods

Patients and setting

Women who underwent breast cancer surgery in our hospital between October 2011 and December 2011 were invited to take part in a follow-up survey in 2012 and 2013 during a postoperative outpatient clinic visit. Patients were eligible for this study if they were ≥ 18 years of age, underwent surgery for breast cancer with a postoperative period of between 13 and 18 months, and agreed to participate. Patients were excluded if they underwent surgery for breast cancer twice or more on the same side, had stage IV or recurred breast cancer, had previous shoulder pathology before breast cancer surgery, or had another cancer (except thyroid cancer) or disease such as rheumatoid arthritis that could affect the study results. In total, 284 patients agreed to participate in the study and informed consent was obtained. Of these, 13 patients were excluded during the screening process based on the exclusion criteria. Thus, 271 patients were included in the final cohort. This study was approved by the institutional review board of our hospital (IRB No. 2012–0783).

Evaluation of adhesive capsulitis

Any history of shoulder pain, adhesive capsulitis diagnosis after breast cancer surgery, and limitation of shoulder ROM were recorded from patient interviews and medical records. Shoulder ROM was measured for forward flexion, abduction, and external rotation of both arms using a goniometer while the patient was sitting. Flexion and abduction were measured while the examiner elevated the patient's arm in the sagittal and coronal planes of the trunk, respectively. External rotation was measured at 0° shoulder abduction and 90° elbow flexion. A restriction of ≥ 30° compared with the sound side was regarded as positive for restriction in the ROM of each direction [9]. If the sound side had a ROM restriction, the degree of restriction was defined based on the normal value, 180° for flexion and abduction and 90° for external rotation. Current adhesive capsulitis was defined as restriction of external rotation and one or more additional directional restrictions with history of shoulder pain or discomfort at examination. Cumulative adhesive capsulitis was defined as current adhesive capsulitis or previous history of adhesive capsulitis diagnosis based on patient interviews and medical records after breast cancer surgery, even if the patient did not meet the definition of current adhesive capsulitis.

Assessment of demographic factors

Age at surgery was categorized into < 40, 40–49, 50–59, and ≥ 60 years. Body mass index was calculated as the weight divided by the height squared (kg/m^2). Obesity was defined as a body mass index over 25 kg/m^2.

Assessment of comorbidities and breast cancer treatments

Comorbidities and breast cancer treatments were recorded from patient interviews and medical records. Diabetes and history of thyroid surgery were recorded. Type of breast cancer surgery was categorized as breast-conserving surgery, mastectomy, or mastectomy with reconstruction. Lymph node dissection was categorized as no dissection or sentinel node dissection and axillary node dissection. History of chemotherapy, radiotherapy, hormone therapy, and targeted therapy were also recorded. The cancer stage was categorized as 0–1, 2, or 3. Lymph node involvement was also recorded and the N stage was dichotomized as stage 0–1 or 2–3 in univariate regression analysis.

Statistical analysis

Univariate logistic regression analysis was used to assess the association between cumulative or current adhesive capsulitis and covariables such as demographic factors, comorbidities, type of breast cancer treatment, and breast cancer stage. Multivariate logistic regression analysis was used to assess the risk factors for cumulative and current adhesive capsulitis. Patients with a history of adhesive capsulitis after breast cancer surgery without current restriction were excluded from the analysis of current adhesive capsulitis. Age at surgery, obesity, diabetes, type of surgery, axillary lymph node dissection, chemotherapy, radiotherapy, hormone therapy, and targeted therapy were included as covariables in multivariate regression analysis. Because the type of cancer treatment is determined by the stage of the disease, the cancer stage and N stage were not included in the multivariate logistic regression analyses. PASW Statistics 18 (SPSS Inc., Chicago, IL) was used for all analyses. A p value < 0.05 was considered to be statistically significant.

Results

The mean age of the 271 study patients was 48.0 years and 179 patients (66.1%) belonged to the 40–59-year-old age group. Regarding the cancer stage, 122 patients (45.0%) had stage I cancer and 104 (38.4%) had stage II cancer. In addition, 52 patients (19.2%) underwent mastectomy and 37 patients (13.7%) underwent mastectomy with reconstruction. After a mean postoperative observation time of 16.6 ± 1.4 months, 28 (10.3%) and 21 (7.7%) patients had cumulative and current adhesive capsulitis, respectively (Table 1).

By univariate logistic regression analysis (Table 2), the risk of cumulative adhesive capsulitis was higher in the patients aged 50–59 years (odds ratio [OR], 7.286; 95% confidence interval [CI], 1.596–33.250), those who underwent mastectomy (OR, 4.171; 95% CI, 1.691–10.285) or mastectomy with reconstruction (OR, 3.009; 95% CI, 1.036–8.735) and those with a history of thyroid surgery (OR, 5.712; 95% CI, 1.288–25.332). Analysis of current adhesive capsulitis showed a similar trend. The risk of current adhesive capsulitis was higher in patients aged 50–59 years (OR, 10.018; 95% CI, 1.249–80.346), those who underwent mastectomy (OR, 6.951; 95% CI, 2.389–20.224) or mastectomy with reconstruction (OR, 4.597; 95% CI, 1.321–15.996) and those with a history of thyroid surgery (OR, 7.933; 95% CI, 1.754–35.891).

By multivariate logistic analyses (Table 3), the risk of cumulative and current adhesive capsulitis was higher in patients aged 50–59 years (OR, 9.912; 95% CI, 1.790–54.880; and OR, 12.395; 95% CI, 1.187–129.444, respectively) and those who underwent mastectomy (OR, 6.805; 95% CI, 1.800–25.733; and OR, 9.645; 95% CI, 2.075–44.829, respectively) or mastectomy with reconstruction (OR, 13.122; 95% CI, 2.488–69.218; and OR, 20.075; 95% CI, 2.873–140.261, respectively). Radiotherapy was associated with a nonsignificant increase in the risk of the development of cumulative adhesive capsulitis (OR, 3.439; 95% CI, 0.835–14.168).

Table 1 Subject demographics and characteristics ($N = 271$)

Characteristics	Number or Mean	% or SD
Age at surgery (years)		
Mean	48.0	9.9
< 40	53	19.6
40–49	107	39.5
50–59	72	26.6
≥ 60	39	14.4
Follow-up time (months)	16.6	1.4
BMI, kg/m^2	23.2	3.2
Obesity	62	22.9
Diabetes	7	2.6
Thyroid surgery	8	3.0
Type of breast cancer surgery		
BCO	182	67.2
Mastectomy	52	19.2
Mastectomy with reconstruction	37	13.7
Lymph node dissection		
No or SLNB	184	67.9
ALND	87	32.1
Chemotherapy	150	55.4
Radiotherapy	198	73.1
Hormone therapy	215	79.3
Targeted therapy	31	11.4
Stage of cancer		
0	15	5.5
I	122	45
II	104	38.4
III	30	11.1
Lymph node involvement	90	33.2
Cumulative adhesive capsulitis	28	10.3
Current adhesive capsulitis	21	7.7

Abbreviations: *ALND* axillary lymph node dissection, *BCO* breast-conserving operation, *BMI* body mass index, *SD* standard deviation, *SLNB* sentinel lymph node biopsy

Discussion

We have investigated the prevalence and risk factors of adhesive capsulitis after breast cancer treatment. Most previous studies evaluated the restriction of motion without taking into account the underlying causative condition [3, 4, 10–12]. Additionally, many of these earlier studies only measured flexion and abduction ROM [3, 11, 12]. Pectoralis tightness, defined as a reduction in shoulder flexion and horizontal abduction without reduced external rotation [13], is the major cause of ROM restriction after breast cancer surgery [14], typically developing in the early postoperative period. However, adhesive capsulitis shows a pronounced restriction of external rotation, with global restriction and insidious onset shoulder pain [5, 6]. It is also expected to show a delayed onset with synovial inflammation and subsequent capsular fibrosis [8]. Intraarticular corticosteroid injection confers rapid pain relief and helps the early recovery of ROM in early-phase adhesive capsulitis [15]. Therefore, identification of the prevalence and risk factors of adhesive capsulitis in breast cancer patients is worthwhile given its distinct pathomechanism and treatment method from other causes of ROM restriction.

Our current analysis indicated that the type of breast cancer surgery was the strongest risk factor for adhesive capsulitis development. In particular, mastectomy was found to increase the risk of adhesive capsulitis. This finding is consistent with previous studies reporting increased shoulder morbidity after mastectomy [3, 11, 14]. Moreover, our results showed that reconstruction with mastectomy seems to additionally

Table 2 Univariate logistic regression analysis for cumulative and current adhesive capsulitis

	Cumulative adhesive capsulitis (N = 271)			Current adhesive capsulitis (N = 264)		
	OR	95% CI	p value	OR	95% CI	p value
Age at surgery (years)						
< 40	1.000			1.000		
40–49	1.785	0.358–8.905	0.480	3.06	0.359–26.105	0.307
50–59	7.286	1.596–33.250	0.010	10.018	1.249–80.346	0.030
≥ 60	2.125	0.338–13.372	0.422	4.25	0.425–42.519	0.218
Obesity	0.911	0.352–2.357	0.847	1.336	0.495–3.604	0.568
Diabetes	1.463	0.170–12.611	0.729	1.975	0.226–17.222	0.538
Type of breast cancer surgery						
BCO	1.000			1.000		
Mastectomy	4.171	1.691–10.285	0.002	6.951	2.389–20.224	<0.001
Mastectomy with reconstruction	3.009	1.036–8.735	0.043	4.597	1.321–15.996	0.017
ALND	1.198	0.528–2.716	0.666	1.078	0.418–2.778	0.877
Chemotherapy	0.923	0.421–2.023	0.842	1.067	0.433–2.625	0.888
Radiotherapy	0.755	0.325–1.754	0.513	0.477	0.192–1.185	0.111
Hormone therapy	0.950	0.366–2.468	0.916	0.829	0.290–2.372	0.727
Targeted therapy	1.333	0.430–4.134	0.618	1.882	0.590–6.007	0.285
Thyroid surgery	5.712	1.288–25.332	0.022	7.933	1.754–35.891	0.007
Stage of breast cancer						
0–I	1.000			1.000		
II	1.015	0.426–2.415	0.974	0.923	0.339–2.516	0.876
III	1.908	0.624–5.831	0.257	1.984	0.576–6.833	0.278
N stage						
0–1	1.000			1.000		
2–3	1.814	0.635–5.181	0.266	1.964	0.614–6.281	0.255

Abbreviations: *ALND* axillary lymph node dissection, *BCO* breast-conserving operation, *CI* confidence interval, *OR* odds ratio

increase the risk compared with mastectomy alone. Mastectomy does not directly damage the glenohumeral joint. However, pain, protective posture, scar formation, and tension of the soft tissue after surgery with a larger extent can cause immobility and alteration of the shoulder girdle alignment [13]. Alterations of the shoulder girdle motion and muscle performance after breast cancer treatment were reported in previous studies [16–18]. It is reasonable to expect that a more extensive surgery would have greater effects on these changes. Yang et al. [14] reported greater pectoralis muscle tightness after mastectomy compared with breast-conserving surgery. These biomechanical changes could cause impingement and stress of the joint capsule, resulting in secondary adhesive capsulitis.

Radiotherapy might cause fibrosis of the shoulder joint capsule and chest wall [19–21], leading to adhesive capsulitis. However, in our present study, there was no definite relationship found between radiotherapy and adhesive capsulitis development, although radiotherapy was observed to be associated with a nonsignificant increase in the risk of cumulative adhesive capsulitis. A previous systematic review has reported increased upper extremity morbidity with more extensive radiotherapy [22]. However, other studies have reported no ROM restriction after radiotherapy [12, 22]. These discrepancies might be due to differences in the morbidity under investigation and the radiotherapy extent and dose. We did not subdivide radiotherapy according to extent and dose in our current investigation and this limitation, and the strong effects of surgery, might have obscured the effects of radiotherapy. Further studies with a greater number of patients would likely be helpful when investigating the effects of radiotherapy on adhesive capsulitis.

Adhesive capsulitis typically occurs in those aged 40 to 60 years in the general population [5, 6, 23]. The risk of adhesive capsulitis was also increased in those aged 50 to 59 years in our study. Moreover, Kootstra et al. [24] reported decreased shoulder ROM in breast cancer survivors aged around 56 years. It seems therefore that age also affects the development of adhesive capsulitis in individuals undergoing

Table 3 Multivariate logistic regression analyses for cumulative and current adhesive capsulitis

	Cumulative adhesive capsulitis ($N = 271$)			Current adhesive capsulitis ($N = 264$)		
	OR	95% CI	p value	OR	95% CI	p value
Age at surgery (years)						
< 40	1.000			1.000		
40–49	2.324	0.426–12.667	0.330	3.71	0.393–34.996	0.252
50–59	9.912	1.790–54.880	0.009	12.395	1.187–129.444	0.035
≥ 60	3.788	0.483–29.712	0.205	7.568	0.550–104.076	0.130
Obesity	0.655	0.218–1.966	0.451	1.007	0.317–3.203	0.990
Diabetes	2.555	0.253–25.777	0.426	5.324	0.492–57.601	0.169
Type of breast cancer surgery						
BCO	1.000			1.000		
Mastectomy	6.805	1.800–25.733	0.005	9.645	2.075–44.829	0.004
Mastectomy with reconstruction	13.122	2.488–69.218	0.002	20.075	2.873–140.261	0.002
ALND	1.061	0.306–3.676	0.926	0.763	0.191–3.053	0.703
Chemotherapy	0.600	0.174–2.068	0.418	0.709	0.174–2.893	0.631
Radiotherapy	3.439	0.835–14.168	0.087	2.546	0.553–11.729	0.231
Hormone therapy	0.981	0.333–2.892	0.972	0.860	0.251–2.947	0.810
Targeted therapy	1.411	0.347–5.747	0.631	2.331	0.518–10.495	0.270
Thyroid surgery	4.009	0.668–24.063	0.129	5.452	0.820–36.246	0.079

Abbreviations: *ALND* axillary lymph node dissection, *BCO* breast-conserving operation, *CI* confidence interval, *OR* odds ratio

breast cancer treatment, as in the general population. Hence, care should be taken when managing breast cancer survivors aged in their 50s to ensure early diagnosis and proper treatment of this disorder.

In adhesive capsulitis, the ROM is gradually restricted in the freezing stage and improves in the thawing stage [8, 25]. In addition, ROM can be improved by several treatments, such as stretching exercises and steroid injections [26, 27]. Therefore, a cross sectional study might lose the improved adhesive capsulitis patients. However, for better risk evaluation, these patients should be included. Accordingly, we here investigated the previous diagnosis of adhesive capsulitis after breast cancer treatment using patient interviews and medical records. However, there is a possibility of bias due to different diagnosis methods between previous and current adhesive capsulitis diagnoses. Therefore, we performed separate regression analysis, based on the diagnosis of cumulative and current adhesive capsulitis. Although some odds ratio differences were observed, the results of the two sets of analyses showed similar trends in both univariate and multivariate regression. Further prospective studies with serial follow-ups are needed to further evaluate risk factors and prognosis.

The type of cancer treatment depends on the stage. Whereas the type of surgery was found in our current univariate regression analysis to be definitely associated with an increased risk of adhesive capsulitis, no such association was seen for cancer stage. In addition, as the type of treatment is expected to more directly impact the shoulder joint than the stage of cancer, we did not include the stage of cancer in our multivariate regression analysis.

We investigated the risk of adhesive capsulitis in our current study, which is unlike most previous studies that just evaluated the limitation of motion or functional morbidity regardless of the specific diagnosis. In addition, our present analysis was performed 13 to 18 months after surgery, not during short-term follow-up, in order to sufficiently evaluate the effect of breast cancer treatment on adhesive capsulitis. However, there were some limitations in our study. First, this was a cross-sectional study and there is a possibility of bias related to the diagnosis of adhesive capsulitis that developed before the study period. Therefore, the diagnosis of previous adhesive capsulitis diagnosis based on patient interviews and medical records might be inaccurate in some cases. Considering this limitation, we analyzed the patients who had cumulative or current adhesive capsulitis separately. Second, we did not subdivide radiotherapy according to extent and dose. A larger sample size would be helpful in this regard for evaluating the effects of radiotherapy in the future. Third, we did not perform ultrasound or magnetic resonance imaging and therefore could not confirm the presence of underlying shoulder pathology to rule out secondary adhesive capsulitis.

Conclusions

Cumulative and current adhesive capsulitis at 13 to 18 months after breast cancer surgery were observed in 10.3% and 7.7% of patients, respectively. Mastectomy is a major risk factor for the development of adhesive capsulitis, and breast reconstruction additionally increases this risk. Patients aged 50–59 years also have an increased risk of adhesive capsulitis. Greater attention should be paid to patients aged in their 50s and those who have undergone mastectomy or mastectomy with reconstruction to improve the early diagnosis and proper treatment of this disorder.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest or financial relationship with the organization that sponsored the research. The authors have had full control of all primary data and agree to allow the journal to review their data if requested.

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