

Influence of and Risk Factors for Axillary Web Syndrome Following Surgery for Breast Cancer

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In this study, we examined whether axillary web syndrome (AWS) in patients with breast cancer following axillary lymph node dissection affects range of motion (ROM), upper extremity function, and quality of life (QOL). The risk factors for AWS were also evaluated in a total of 238 consecutive breast cancer patients following axillary lymph node dissection. At 1, 2, and 3 months after surgery, there were no significant differences between the AWS group and the non-AWS group in upper-limb function or QOL. At 2 months after surgery, shoulder flexion and abduction ROM were significantly higher in the AWS group than in the non-AWS group ($p < 0.05$). Self-training time at home was not significantly different between the groups at 1, 2, or 3 months. Only age was a significant predictor of AWS at 1 month after surgery ($p < 0.05$). The AWS group in the present study did not have worse results for shoulder joint ROM, upper-limb function, and QOL than the non-AWS group. Younger age should be useful for predicting the development of AWS in the early postoperative period.

Key words: breast cancer, axillary web syndrome, age, upper limb function, quality of life

Breast cancer is the most common cancer that affects women and the leading cause of cancer death among them [1]. Surgery is the treatment of choice for patients with breast cancer, and it generally includes sentinel lymph node biopsy or axillary lymph node dissection (ALND). The axillary surgical approach has postoperative morbidity, including early or long-term complications such as axillary web syndrome (AWS), decreased range of motion (ROM) of the arm or shoulder, numbness, pain, and lymphedema [2-6].

AWS has been characterized as the presence of a visible and palpable stretched band underneath the skin, which is taut and painful during shoulder flexion or abduction [7-10]. The cords originate in the axilla and

extend to the medial and upper portions of the arm to the anterior portion of the elbow [8]. Several studies have reported that AWS occurs after a delay of one week post-surgery and resolves within the following three months [7, 11-15]. AWS has been reported to negatively affect shoulder ROM and lymphedema development [6, 16]. Risk factors for AWS may include extensive surgery [6, 17], younger age [5, 17], lower body mass index (BMI) [5, 14, 17], ethnicity, and healing complications [5, 6]. In Japan, there have been no studies on whether AWS is related to decreased ROM of the arm or shoulder, or decreased quality of life (QOL). In addition, the risk factors for the development of AWS in Japan are unclear.

In this study, we examined whether AWS in patients

with breast cancer following ALND affects ROM, upper extremity function, and QOL. Risk factors for AWS were also evaluated.

Methods

Patients and methods. The subjects of this study were 238 consecutive breast cancer patients who underwent ALND at our hospital between November 2013 and December 2016. All subjects were female. Age, BMI, level of lymph node dissection (Level 1, Level 2, and higher), preoperative chemotherapy (yes or no), self-training time at home, shoulder ROM, upper extremity function (disabilities of the arm, shoulder and hand [DASH]), and QOL (EORTC QLQ-C 30) were evaluated.

Ethical approval. This study was approved by the Shikoku Cancer Center Ethics Committee, and written informed consent was obtained from each participant (Approval No. 2018-45).

Rehabilitation program. As preoperative rehabilitation during hospitalization, guidance was given on upper extremity exercises using a prerecorded video on a DVD. In the video, an instructor demonstrated proper movement of the upper extremity. Postoperative rehabilitation was started from the first and second postoperative days with exercise beyond the elbow joint. From the third postoperative day to the day of drain withdrawal, upper extremity ROM exercises were performed within 90 degrees of shoulder joint flexion and abduction. After removal of the drain, shoulder ROM was not restricted, and exercise of the upper extremity and activities of daily living (ADL) were adjusted according to the degree of pain. Patients were also instructed to perform self-training at home with the DVD at least once a day after discharge from the hospital.

Patients who developed AWS at discharge or at 1, 2, or 3 months after surgery were instructed to raise the shoulder joint while flexing the elbow to extend the axilla if they had a strong sense of tension or pain in the upper limbs during the shoulder raising movement in the elbow extension position. In ADL, when participants experienced a sense of tension in the elbow extension position, they were instructed to perform the movement in the elbow flexion position if possible.

Axillary web syndrome assessment. Patients were defined as having AWS in the operated upper extremity

when a cord of tissue was present at 1, 2, or 3 months after surgery.

We evaluated AWS as follows:

- Patients were assessed as having AWS when a cord of tissue was present in the axilla, upper limbs, or trunk during maximum shoulder abduction of the operated upper extremity [18].

- Patients were assessed as having AWS even in the absence of local pain when a cord of tissue was present in the operated upper extremity [18].

- Patients were assessed as having AWS even when there was no restriction in their shoulder ROM when a cord of tissue was present in the operated upper extremity [18].

In this study, the patients were categorized into the AWS group and the non-AWS group.

Quality of life assessment. QOL was measured using an EORTC QLQ-C30 questionnaire [19]. This questionnaire includes items relating to global health status, functional scales (physical, role, emotional, cognitive, and social), and symptom scales (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). EORTC QLQ-C 30 measurements were evaluated at 1, 2, and 3 months after surgery.

Shoulder range of motion test. The ROM test was used to measure active shoulder flexion and abduction 1, 2, and 3 months after surgery.

Evaluation of disabilities of the arm, shoulder and hand. The DASH is a 30-item disability/symptom scale concerning the patient's health status during the preceding week [20]. The 30 items consist of 21 items about the degree of difficulty in performing different physical activities due to arm, shoulder, or hand problems, 5 items about the severity of the symptoms, and 4 items concerning the effects of the upper extremity problem on social activities, work, sleep, and self-image. DASH was administered at 1, 2, and 3 months after surgery.

Self-training time at home. Self-training time at home was investigated at 1 month, 2 months, and 3 months after surgery. The one month measurement included all self-training from discharge to 1 month after surgery, the 2 month measurement included all self-training from 1 month to 2 months after surgery, and the 3 month measurement included all self-training from 2 months to 3 months after surgery. The average daily self-training time at home was examined within

each period.

Statistical analysis. For shoulder joint ROM, DASH, and EORTC QLQ-C 30 comparisons between the AWS and non-AWS group were evaluated using Student's *t*-test, the chi-squared test, and the Mann-Whitney *U* test. To identify factors predictive of AWS at 1, 2, and 3 months after surgery, univariate analysis was carried out using Student's *t*-test, the chi-squared test, and the Mann-Whitney *U* test, with age, BMI, level of lymph node dissection, and preoperative chemotherapy as variables. Next, for items with $p < 0.1$ on univariate analysis, logistic regression analysis was used to identify the best independent predictor of AWS at 1, 2, and 3 months after surgery.

All statistical tests were two-sided, with $p < 0.05$ considered significant. Statistical analyses were performed using IBM SPSS Statistics Version 22.0 (IBM, Tokyo).

Results

Occurrence of axillary web syndrome. There were 55, 47, and 23 patients at 1, 2, and 3 months, respectively, in the AWS group. There were 183, 191, and 215 patients at 1, 2, and 3 months, respectively, in the non-AWS group.

Comparisons of the shoulder joint range of motion, DASH, and EORTC QLQ-C 30 between groups.

Table 1 shows the differences in self-training time at home, shoulder ROM, DASH, and QLQ-C 30 between the AWS and non-AWS groups at 1, 2, and 3 months after surgery.

At 1 month after surgery, there were no significant differences between the AWS and the non-AWS groups in self-training time at home, shoulder ROM, DASH, or QLQ-C 30.

At 2 months after surgery, shoulder flexion ROM and abduction ROM were significantly higher in the AWS group than in the non-AWS group ($p < 0.05$). Self-training time at home, DASH, and QLQ-C 30 were not significantly different between the groups.

At 3 months after surgery, there were no significant differences between the AWS and non-AWS groups in self-training time at home, shoulder ROM, DASH, or QLQ-C 30.

Factors predicting axillary web syndrome. On univariate analysis, age showed a significant difference between the AWS and non-AWS groups at one month after surgery (Table 2). Age was the only significant predictor of AWS at one month after surgery ($p < 0.05$) (Table 3). There were no items that showed significant differences at two and three months after surgery.

Table 1 Comparison of range of motion test, upper extremity function, and QOL between the AWS and non-AWS groups at one, two, and three months after surgery

Variable	One month (n=238)			Two months (n=238)			Three months (n=238)		
	AWS group	Non-AWS group	<i>p</i> value	AWS group	Non-AWS group	<i>p</i> value	AWS group	Non-AWS group	<i>p</i> value
Self- training time (times) ^{a)}	24.4 ± 19.0	26.0 ± 23.0	0.921	18.4 ± 24.0	15.2 ± 14.0	0.685	7.0 ± 8.6	11.0 ± 12.0	0.152
DASH (scores) ^{a)}	23.2 ± 11.6	21.5 ± 13.9	0.187	20.0 ± 16.1	18.6 ± 15.4	0.659	15.6 ± 12.4	15.4 ± 13.1	0.790
ROM (degrees) ^{a)}									
Shoulder flexion	142.6 ± 17.8	137.8 ± 18.5	0.086	156.5 ± 11.0	149.0 ± 16.0	0.002	153.3 ± 12.5	154.5 ± 14.2	0.484
Shoulder abduction	137.5 ± 23.8	134.2 ± 24.6	0.421	156.0 ± 17.2	147.9 ± 20.5	0.008	155.0 ± 15.2	154.7 ± 17.5	0.756
QLQ-C 30 (scores) ^{a)}									
Global health status/QOL	62.3 ± 19.1	64.2 ± 21.3	0.506	65.9 ± 21.9	62.9 ± 22.5	0.357	59.8 ± 22.8	66.4 ± 24.2	0.175
Physical function	85.3 ± 11.1	84.3 ± 14.1	0.939	85.2 ± 14.1	86.3 ± 14.0	0.668	89.0 ± 7.7	87.5 ± 12.4	0.923
Role function	73.5 ± 19.0	76.1 ± 19.0	0.355	75.9 ± 26.5	77.4 ± 22.9	0.945	81.9 ± 15.8	81.8 ± 22.8	0.542
Emotional function	76.9 ± 16.6	76.6 ± 19.6	0.729	82.6 ± 17.3	82.7 ± 17.1	0.979	88.8 ± 11.7	85.2 ± 16.2	0.439
Cognitive function	86.4 ± 14.4	86.0 ± 16.7	0.793	83.3 ± 17.0	84.1 ± 18.6	0.616	86.2 ± 15.6	84.8 ± 18.4	0.924
Social function	79.4 ± 21.7	81.9 ± 21.0	0.423	75.2 ± 26.5	80.6 ± 20.7	0.307	82.6 ± 23.3	84.2 ± 21.8	0.840
Fatigue	26.5 ± 16.9	27.3 ± 19.8	0.885	27.9 ± 17.2	27.1 ± 20.5	0.558	29.0 ± 19.2	25.6 ± 18.4	0.436
Nausea/Vomiting	1.5 ± 7.4	1.7 ± 6.5	0.609	5.6 ± 14.2	4.5 ± 11.8	0.537	5.8 ± 17.8	3.8 ± 11.4	0.782
Pain	31.6 ± 14.4	29.3 ± 16.9	0.214	16.3 ± 14.0	22.0 ± 18.5	0.078	14.5 ± 11.6	19.4 ± 20.6	0.473
Dyspnea	7.9 ± 14.3	10.3 ± 16.6	0.402	14.8 ± 19.5	11.5 ± 20.0	0.207	11.6 ± 19.1	12.6 ± 18.7	0.732
Insomnia/sleep	20.0 ± 20.9	21.0 ± 23.6	0.967	21.5 ± 24.8	24.4 ± 27.3	0.600	17.4 ± 17.0	20.8 ± 23.7	0.749
Appetite loss	7.3 ± 16.6	6.7 ± 15.6	0.912	16.3 ± 24.2	13.4 ± 22.3	0.441	14.5 ± 24.3	12.1 ± 19.6	0.880
Constipation	12.7 ± 18.7	12.0 ± 18.3	0.734	21.5 ± 30.3	17.8 ± 22.8	0.772	23.2 ± 32.5	15.3 ± 21.9	0.319
Diarrhea	6.1 ± 18.2	3.9 ± 10.7	0.744	7.4 ± 15.7	10.8 ± 22.4	0.512	7.2 ± 17.3	6.8 ± 16.8	0.895
Financial difficulties	13.3 ± 19.9	19.2 ± 25.0	0.268	22.2 ± 26.6	17.8 ± 22.5	0.374	18.8 ± 22.1	14.3 ± 20.9	0.192

Table 2 Results of univariate analysis to extract risk factors for AWS at 1 month after surgery

Variable	AWS group (n=55)	Non-AWS group (n=183)	p value
Age (y) ^{a)}	52.0 ± 11.0	57.7 ± 12.4	0.002
BMI (kg/m ²) ^{a)}	22.5 ± 3.6	23.2 ± 4.0	0.290
Time for drain removal (days) ^{a)}	5.0 ± 1.8	4.9 ± 1.5	0.982
Level of lymph node dissection (I / II / III) ^{b)}	41/10/4	143/25/15	0.634
Resection of pectoralis minor muscle (yes or no) ^{b)}	1/54	8/175	0.385
Neoadjuvant chemotherapy (yes/no) ^{b)}	19/36	50/133	0.302

Table 3 Risk factors of AWS determined by logistic regression analysis at one month after surgery

Variable	Odds ratio (95%CI)	p value
Age	0.961 (0.935-0.987)	0.003

Discussion

AWS has been reported to occur in 5.2-72% of patients following ALND [17,21]. Several studies showed that AWS occurred 1-8 weeks after axillary surgery [8, 16], and AWS has been shown to resolve within three months after surgery [8, 22]. In addition, physiotherapy for AWS has been shown to shorten the natural course of the syndrome to 6-8 weeks [14]. In the present study, the rate of AWS was 23.1%, 19.7%, and 9.7% at 1, 2, and 3 months after surgery, respectively; the rate showed a gradual decrease. After surgery, the present breast cancer patients were encouraged to perform self-training at home, but AWS occurred even three months after surgery. Therefore, patients may need exercise therapy and upper extremity function assessment beyond 3 months after discharge for breast cancer surgery.

Several studies showed reduced active shoulder flexion and abduction in patients with AWS [16, 23]. In our research, there were no significant differences in active shoulder flexion ROM and abduction ROM between the AWS group and the non-AWS group at 1 and 3 months after surgery. At 2 months after surgery, the ROMs of shoulder flexion and abduction were significantly higher in the AWS group than in the non-AWS group.

In other studies, rehabilitation interventions have been reported to be effective in improving AWS [24]. Patients with AWS tend to reduce the time they spend exercising due to a sense of tension and pain. In the present study, the patients were instructed to perform vigorous rehabilitation at discharge and 1, 2, and 3

months after surgery. Also, patients who developed AWS at 1, 2, and 3 months after surgery were given advice on exercise and ADL according to their condition. As a result, self-training time at home showed no significant differences between the AWS and non-AWS groups at 1, 2, and 3 months after surgery. This means the AWS group did not show a decrease in shoulder ROM compared to the non-AWS group at 1 and 3 months after surgery. Furthermore, an increase in shoulder ROM was observed in the AWS group at 2 months after surgery. Even patients who developed AWS may have also attained a good result by self-training at home.

Studies have reported on functional activities after breast surgery, though none related these findings to AWS [25, 26]. In our research, there was no significant difference in the DASH between the AWS and non-AWS groups. AWS causes symptoms such as a sense of tension or pain on shoulder flexion while extending the elbow and axilla. In raising the shoulder joint, elbow joint flexion reduces AWS symptoms. In the DASH assessment, many of the items related to the degree of difficulty in performing different physical activities due to arm, shoulder, or hand problems can be performed even in elbow flexion. Thus, this may explain why the present study found no significant differences between the AWS and non-AWS groups.

Several studies have shown that AWS caused patient anxiety and fear due to poor understanding of the complication [7, 24]. In this study, QOL was not significantly different between the AWS and non-AWS groups at 1 to 3 months postoperatively. There were no significant differences in upper extremity function between groups. Therefore, in the patients of the present study, the effect on QOL of the occurrence of AWS was likely low.

The risk factors for developing AWS have been reported to be ALND, lower BMI, and younger age

[5, 6, 14, 17]. It is possible that age and BMI are related, since older people are more likely to have a higher BMI [14]. In the present study, the only risk factor for developing AWS at one month postoperatively was age, and no factors were observed at 2 and 3 months in breast cancer patients following ALND. In patients with breast cancer after ALND, the reason why only young age affects AWS is not clear, but younger age may be useful for predicting the development of AWS in the early postoperative period. Also, in this study, age was not seen as a factor that was linked to the occurrence of AWS at 2 or 3 months post-surgery. AWS showed a tendency of gradual improvement in the three months following surgery. Age can affect the early occurrence of AWS but may not be a factor linked with improving AWS.

There were some limitations associated with this study. First, because all subjects were patients who had participated in the Rehabilitation program for three months, our results do not reflect the effect on patients who do not participate in a Rehabilitation program. Second, in our research, the effect of AWS was examined in patients with breast cancer, but a useful method for preventing and improving AWS remains to be clarified. Third, this research was conducted at a single facility, and the results of collaborative research with other research facilities could be different.

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