

Exploring the Relationship between
Axillary Web Syndrome Characteristics and Physical Function

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Abstract

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Complications following breast cancer treatment are often given significantly less attention when assessing patients in favour of emphasizing survival rate, yet they represent a significant burden to survivors and should be treated accordingly. While lymphedema is the most prominent complication to occur postoperatively, axillary web syndrome (AWS) has emerged as a significant complication, leading to restrictions in range of motion, pain and an overall lower quality of life. While AWS is still an emerging topic with minimal background research, current findings agree that movement and function are restricted in the affected upper limb. The primary goal of this study is to examine the relationship between AWS and physical function; the secondary goal was to identify any other factors that may impact the condition. A novel scoring system was used alongside a validated assessment tool, the QuickDASH questionnaire, to identify any possible relationships between the severity of AWS and physical function. We hypothesized that a higher score on the AWS severity grading tool would be linked to higher scores on the QuickDASH questionnaire (decreased physical function). Pearson correlations were used to identify any meaningful relationships between the variables of interest, and independent sample t-tests were then used to analyze differences in subgroups. Our findings indicate a statistically significant correlation between AWS severity and QuickDASH scores, where increased severity is associated with decreased physical function. Furthermore, our analyses show that pain is a notable factor when determining severity, highlighting the importance of assessing this specific variable.

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Contribution of Authors

Lingchung Tam conducted data collection, performed statistical analyses, and was responsible for manuscript writing, editing, and final submission. Dr. Robert D. Kilgour contributed to study design, secured study funding, provided study supervision, and assisted with manuscript editing. All authors reviewed and approved the final manuscript.

Table of Contents

List of figures.....	vii
List of tables.....	viii
Introduction.....	1
Background and Context.....	1
Literature Review.....	2
Significance.....	6
Research questions and hypotheses.....	8
Materials and Methods.....	9
Results.....	11
Demographic characteristics.....	11
AWS grading tool.....	12
Morphological summary.....	20
Functional summary.....	20
Pain summary.....	20
QuickDASH scoring and relationships.....	21
Discussion.....	25
Conclusion.....	31
Limitations.....	31
Future Directions.....	32
References.....	34
Appendix A – AWS Scoring System.....	40
Appendix B – QuickDASH Questionnaire.....	41

List of figures

Figure 1: Relationship between Total Severity Score and Total QuickDASH Score in AWS.....	21
Figure 2: Total Severity Score Differences in Individuals with and without Pain.....	22
Figure 3: Relationship between Pain VAS and QuickDASH Pain Subset Scores	23

List of tables

Table 1: Participant Characteristics	12
Table 2. Distribution of Cords by Anatomical Locations	14
Table 3. Variation in Cord Thickness by Anatomical Locations.....	15
Table 4. Variation in Cord Depth by Anatomical Locations	16
Table 5. Presence of Swelling by Anatomical Locations.....	17
Table 6. Distribution of Range of Motion Restriction in Shoulder Abduction	17
Table 7. Distribution of Range of Motion in Shoulder Flexion Restriction	18
Table 8. Distribution of Range of Motion in Elbow Extension Restriction.....	18
Table 9. Distribution of Range of Motion in Hand and Wrist Restriction	18
Table 10. Distribution of Pain Scores	18
Table 11. Distribution of ADL Limitation Impact Scores.....	19
Table 12: Total Scores for All AWS Criteria.....	19
Table 13: Distribution of AWS Severity Scores.....	19

Introduction

Background and Context

Research surrounding breast cancer has made remarkable progress in the past decades, leading to earlier detection, more effective treatments and overall improvements in patient prognosis. The overall 5-year survival rate is currently in the 90% range (Nardin et al., 2020). While survival rates have increased significantly, complications following breast cancer treatment have become important factors that many survivors must grapple with throughout recovery.

Breast cancer-related lymphedema is one of the primary complications arising from breast cancer treatment, with an estimated incidence rate of 21.4% (DiSipio et al., 2013). Lymphedema is an accumulation of protein-rich interstitial fluid known as lymph, which can be localized to one region of the body or generalized in one specific tissue, leading to the formation of edema in the affected regions (Sakorafas et al., 2006). This condition results from a dysfunction of the lymphatic system: in breast cancer-related lymphedema, the cancer treatments involve the surgical removal of axillary lymph nodes to prevent metastasis of the cancer (Bembenek & Schlag, 2000). The removal of these lymph nodes compromises lymphatic drainage, leading to flow disruption and fluid buildup in the upper limbs, leading to the hallmark symptom of swelling (Gillespie et al., 2018). The onset of lymphedema typically occurs around 6 to 12 months following surgery and may depend on the type and invasiveness of the surgery received by the patient (McDuff et al., 2016). Lymphedema in the upper extremities can be described using limb volumes, with a difference of 10% or more between the affected and unaffected limb as a diagnostic benchmark value (Hidding et al., 2018).

There is currently no cure for lymphedema, thus requiring lifelong attention and management from breast cancer survivors. The removal of axillary lymph nodes and disruptions caused within the lymphatic system following surgery are the main causes behind the chronic nature of lymphedema, primarily stemming from the inability of the lymphatic system to regenerate the removed or damaged structures (Blum et al., 2013). The swelling in the upper limbs can be a major source of discomfort and physical impairment, impacting the quality of life in women during the recovery process (Jaszkul et al., 2023). The increase in limb size can be associated with decreases in range of motion in the shoulder, elbow and wrist, which can affect the performance of everyday tasks (Fu, 2014). While lymphedema is one of the most widely recognized and studied complications following breast cancer surgery, recent findings have highlighted axillary web syndrome as an emerging but underdiagnosed postoperative complication.

Literature Review

Axillary web syndrome (AWS) is a condition first described by Moskovitz et al. in 2001, characterized by a “visible web of axillary skin overlying a palpable cord of tissue”. The nature of the cording is believed to be linked to disruptions caused by surgery to the lymphatic system given its close association with breast cancer and its impact on lymphatic dynamics. The lymphatic system is closely linked to the immune system, serving as a transport system for immune cells, initiating immune responses and filtering foreign antigens that enter the body (Randolph et al., 2017). Stasis of lymph in the limbs results in chronic T-cell inflammation, as demonstrated by a study performed on rat tails where an increased infiltration of CD4⁺T cells in subjects with lymphedema was observed (Avraham et al., 2013). This same study also demonstrated the significance of the differentiation profile of the T cells, where the main driver

behind the initiation of fibrosis was identified as Th2, a subtype of T helper cells (Avraham et al., 2013). Th2 helper cells produce Th2 cytokines, including interleukin-4 (IL-4), IL-5 and IL-13, which are groups of cytokines that play crucial roles in the regulation of immune responses (Nakayama et al., 2017). The fibrosis observed in patients with lymphedema is believed to be caused by the deposition of extracellular matrix by fibroblasts in response to the production of these cytokines (Kokubo et al., 2022). Another important player in the regulation of fibrosis is transforming growth factor-beta 1 (TGF- β 1), which displays an increased expression in tissue affected by lymphedema; Sano et al. (2020) found that TGF- β 1 was produced as a result of immune responses, mainly by macrophages and fibroblasts depending on disease progression leading to accelerated collagen synthesis and fibrotic development of surrounding tissue, mainly in the skin (Sano et al., 2020).

The pathogenesis of AWS is believed to be rooted in the fibrosis of veins and lymphatic vessels in the affected limb (Dinas et al., 2019). A case series by Leduc et al. (2009) conducted on 15 women showed that AWS cord patterns were similar to the organization of brachial lymphatic vessels, emphasizing the significance of the lymphatic origin of the cords. Rashtak et al. further confirm this point in a 2012 study where proliferation of fibroblasts was identified surrounding a lymphatic vessel in the arm of a patient diagnosed with AWS, linking the lymphatic system to the condition. The use of ultrasound imaging to identify specific structures that may be observed in AWS did not yield any definitive results, leading to the conclusion that the cording was in fact due to changes in lymphatic vessel structure and not associated with venous thrombosis (Koehler et al., 2014). While the mechanisms of fibrosis of the lymphatic vessels are not yet definitively defined, the accumulation of proinflammatory markers as described above in the development of lymphedema may be key contributors to the processes.

AWS is most commonly diagnosed in patients who have undergone surgical breast cancer treatment, and the development of the cording occurs most often at two weeks post-surgery (Dinas et al., 2019). It is seen in patients who have undergone axillary lymph node surgery, although a higher incidence of the condition has been observed in patients who have undergone more invasive axillary surgeries, highlighting surgery complexity as a risk factor (Yeung et al., 2015). Research has also shown that the incidence of AWS is higher in patients with a low body mass index (BMI) (Koehler et al., 2015). While the link between this factor and condition development is not yet well defined, a study done by Torres Lacomba et al. (2009) hypothesizes that the increased lipid membranes in the limbs of obese patients may delay lymphatic vessel degradation, reducing the risk of developing AWS. The incidence of AWS varies across literature, ranging from 4 to 85% in patients who have undergone breast surgery; this wide range could be attributed to the novelty and limited exposure of AWS in clinical settings (Yeung et al., 2015). The diagnosis of AWS is done clinically, primarily through the presence or absence of cording: a positive diagnosis is given if there is at least one cord detected through palpation. Limitations in movement are most often observed in the shoulder, particularly when performing shoulder abduction, but can extend distally into the elbow and wrist (Koehler et al., 2015). Symptoms typically center around movement in the affected areas, as well as pain and discomfort when moving the affected limb; many patients reported that while movement was not necessarily restricted, there was a noticeable difference when comparing the feeling before and after the development of cording (Koehler et al., 2018).

AWS and breast cancer-related lymphedema are conditions that are often associated with one another, primarily due to their shared etiology and link to disruptions in the lymphatic system. The development of AWS has been thought to precede that of lymphedema; previous

literature has shown that cording typically appears shortly after surgery, between two to eight weeks postoperatively, while the onset of lymphedema typically occurs several months following surgery (Koehler et al., 2018). However, this suggested timeline is not definitive, since the existence of chronic AWS overlaps the symptoms of lymphedema.

The assessment of AWS varies, often focused on evaluating the restrictions in range of motion associated with the condition. Self-assessments are useful tools that offer an insight into how function is affected in patients' daily lives, since diagnosis of AWS often does not occur at the time of cording development. This delay is likely due to comorbidities following treatment or lack of access to healthcare professionals, particularly due to the clinical nature of the diagnosis (Mullen & Harvey, 2019). The QuickDASH questionnaire, or a shortened version of the Disability of the Arm, Shoulder and Hand questionnaire (DASH), has been proven to be an effective tool in measuring limb function and activities of daily living in breast cancer-related movement restrictions (Leblanc et al., 2014). This questionnaire would be considered as a relevant and adequate instrument in measuring physical impairments associated with AWS given the nature and location of the cording.

The primary form of treatment for AWS is physiotherapy, since the symptoms are mainly related to restrictions in range of motion. Management through physical therapy is provided to primarily aid in restoring any loss of functionality attributed to cording. AWS is a self-limiting condition, where symptoms subside over time, and while treatment for the condition itself is not usually necessary due to its self-limiting nature, management of symptoms is significant to improve patient quality of life (Moskovitz et al., 2001). Exercise, strength training and range of motion exercises are the most common prescriptions, alongside patient education to ensure effective application of techniques (Yang et al., 2020). Additionally, manual lymphatic drainage

can be recommended as a treatment method, since disturbances to lymphatic circulation are linked to AWS development, and this technique can help decrease the accumulation of lymph in the limbs (Cho et al., 2015). A combination of both physical therapy and manual lymphatic drainage has also shown a reduction in physical symptoms and improvements in outcomes, versus only receiving a singular treatment method (Yang et al., 2020). Improvements in range of motion combined with increased lymphatic efficiency may aid in enhancing mobility. Finally, psychological benefits have also been observed following treatment, alleviating patient anxiety that may arise following a diagnosis of AWS (Yang et al., 2020).

Significance

AWS is a relatively new condition, and when comparing it to other complications following breast cancer treatment such as lymphedema, research surrounding the topic is scarce. It is often underreported, or clinicians simply do not assess it due to a lack of knowledge of the condition. There are currently no standard assessment tools or protocols for diagnosis and treatment of AWS, which can impede on the identification of the condition (Nevola Teixeira et al., 2014). Furthermore, a large portion of the existing literature is based on case reports, and while some constant factors can be observed in all cases, there are often small details that can vary from one patient to the next, making it challenging to establish clear diagnostic criteria. Finally, AWS is currently only documented and diagnosed in binary terms, where patients either present with or without cording. This lack of nuance and severity grading results in standardized treatment protocols that may not be adequate for a patient's individual condition. There are no assessment scoring systems post-diagnosis that would measure AWS severity and the many morphological and functional factors that are impacted by AWS. Furthermore, there are no descriptors of the morphology of the cording, such as the integrity of the cords, their location,

and the distribution through the limb. Establishing a standardized assessment and grading system for AWS could greatly improve the visibility of the condition to allow for more personalized treatment plans and ultimately improve patient outcomes. By providing a clear grading system, patients can be stratified based on severity and healthcare professionals can more easily decide the adequate treatment needed depending on how severe AWS is described.

Research questions and hypotheses

This study aimed to investigate the relationship between AWS severity and physical function. Other factors including BMI and the presence of lymphedema were examined to determine their impact on AWS.

The primary objective of this study was to examine the relationship between cord severity and physical function using the novel AWS scoring system and the QuickDASH questionnaire. We hypothesized that an increase in AWS severity, or a higher score on the AWS scoring system, would be associated with a decrease in physical function, or higher scores on the QuickDASH questionnaire.

The secondary objectives of this study were to examine the relationship between AWS severity and other related factors, such as BMI, surgery type, lymph node removal and the presence of lymphedema. We hypothesized that lower BMI, greater surgery invasiveness, thus greater number of lymph nodes removed, and a positive lymphedema diagnosis would all be associated with increased AWS severity, seen as a higher score on the AWS scoring system.

Materials and Methods

This study was a cross-sectional pilot study of adult women who were patients at the McGill University Health Center (MUHC) Lymphedema Clinic in Montreal, Canada. Participants were eligible to participate in the research project if they were aged 18 and older, were fluent in English or French, were able to provide informed consent and were experiencing acute or chronic AWS following breast cancer treatment.

Prior to assessment, participants were asked to fill out a series of questionnaires, including the QuickDASH questionnaire to assess upper limb functional disability (0-100 points). This specific questionnaire was chosen due to its proven effectiveness in measuring limb function and activities of daily living in breast cancer-related movement restrictions.

Height and weight were measured for each participant following the completion of the questionnaires. The participant was then seen by the specialized therapist at the clinic, where bilateral limb volumes were measured. A novel AWS scoring sheet was then used to assess different factors of interest; a separate study on the reliability of the tool is currently being performed. The creator of this tool has over 20 years of therapeutic experience in addressing breast cancer-related complications, was the one who designed the scoring system and assessed all the participants for this study. Participants were evaluated on the morphology of the cording, including the number, thickness, depth and swelling of cords, as well as functional measures such as shoulder abduction, shoulder flexion, elbow extension and hand and wrist restriction. In the morphological component, there was subjective scoring for the number of cords (0-2 points), cord thickness (0-3 points), cord depth (0-3 points) and presence of swelling (0-1 points) at the various regions of the arm including the axilla, upper arm, elbow, forearm, wrist, hands, fingers as well as the trunk and breast, yielding a score out of 54 points. The functional measures

included the subjective scores for the range of motion (ROM) surrounding shoulder abduction (0-10 points), flexion (0-10 points), elbow extension (0-3 points), and hand /wrist restriction (0-3 points), with a component score out of 26 points. Finally, participants were asked to rate their pain attributed to AWS using a visual analog scale (0-10 points) and if the impact of any activities of daily living (ADL) limitations related to the condition were observed (0-10 points). The total AWS scores were accumulated to construct a severity table with the level of severity ranging from very mild (1-5 points) to severe (>51 points).

Medical charts were made available to obtain further patient information, including past medical history, types of cancer treatment (surgery, chemotherapy, radiation), types of surgery (breast and axilla surgeries) and other comorbidities.

The data was organized using Microsoft Excel, and statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 30.0. Descriptive statistics were conducted on variables of interest, including age, BMI, breast surgery type and axillary surgery type to examine the distribution of the data. The mean scores of different components on the AWS grading sheet were examined, and the relationships between different variables were analyzed using Pearson correlations, assuming that the data was normally distributed. The relationships of interest included links between AWS severity score and QuickDASH score, visual analog scale (VAS) pain scale on the AWS severity scoring sheet and the “pain” subset questions on the QuickDASH questionnaire, AWS severity scores and axilla surgery type and AWS severity scores and BMI.

Results

Demographic characteristics

This study analyzed data from 25 women who have completed breast cancer treatment and have been diagnosed with axillary web syndrome. A Shapiro-Wilk test was performed and indicated that data was normally distributed ($p>0.05$). Participant characteristics are presented in Table 1. The age range of participants was 28 to 81 years old with a mean age of 60.5 (SD=13.8). The BMI range of participants was 18.7 to 43.1 with a mean of 28.4 (SD=4.9). Seventeen women underwent a mastectomy while eight underwent a lumpectomy. Nineteen participants had axillary lymph node dissection (ALND) and six had sentinel lymph node biopsy (SLNB). The data surrounding the number of lymph nodes removed during axilla surgery was available for 17 out of the 25 participants; the mean number of lymph nodes removed was 12 (SD=7) in ALND and 3 (SD=0.7) in SLNB. Nineteen participants underwent chemotherapy and twenty-two received radiation therapy. Five out of the 25 women presented with lymphedema in the affected arm, characterized by a difference in arm volume of 10% or more. The dominant arm was affected with AWS in 48% (n=12) of the participants.

An analysis between the lymphedema and non-lymphedema groups was performed to assess any difference in measures: independent sample t-tests between each group were conducted on variables of interest, including total AWS severity scores and the associated subsections, QuickDASH scores and BMI. Results yielded no significant differences between groups.

Table 1: Participant Characteristics

Characteristic	Mean (SD)
Age	60.5 (13.8)
BMI	28.4 (4.9)
Lymph nodes removed	
ALND	12 (7)
SLNB	3 (0.7)
	n (%)
AWS side	
Ipsilateral	12 (48)
Contralateral	12 (48)
Ambidextrous	1 (4)
Breast surgery	
Mastectomy	17 (68)
Lumpectomy	8 (32)
Type of node removal	
ALND	19 (76)
SLNB	6 (24)
Chemotherapy	
Yes	19 (76)
No	6 (24)
Radiation	
Yes	22 (88)
No	3 (12)
Hormonotherapy	
Yes	14 (56)
No	7 (28)
Lymphedema	
Yes	5 (25%)
No	20 (75%)

AWS grading tool

The grading sheet was separated into different sections with corresponding scores, consisting of a morphological component (mean=20.2, SD=6.0) (see Tables 2 to 5), a functional component (mean=3.3, SD=4.6) (see Tables 6 to 9), a pain component (mean=2.1, SD=2.3) (see Table 10) and an activities of daily living (ADL) component (mean=1.7, SD=2.1) (see Table 11). A compilation of every component including the weight of each element can be seen in Table 12.

All mean AWS criteria scores were below 50% (range=3-46%) of the maximum score. The total severity score was calculated using the sum of the scores of each component: the range of the total severity score on the AWS grading tool was 12 (mild severity) to 51 points (severe severity) with a mean point score of 27.2 (SD=10) (see Table 13). The mean total score reflects an overall moderate severity (26-50 points) among the participants.

Table 2. Distribution of Cords by Anatomical Locations

Anatomical locations	Scoring for number of cords	Number and percentage of participants
Axilla		
None	0	0/25 (0%)
Single	1	12/25 (48%)
Multiple	2	13/25 (52%)
Upper Arm		
None	0	0/25 (0%)
Single	1	14/25 (56%)
Multiple	2	11/25 (44%)
Elbow		
None	0	16/25 (64%)
Single	1	9/25 (36%)
Multiple	2	0/25 (0%)
Forearm		
None	0	19/25 (76%)
Single	1	6/25 (24%)
Multiple	2	0/25 (0%)
Wrist		
None	0	24/25 (96%)
Single	1	1/25 (4%)
Multiple	2	0/25 (0%)
Hand/Fingers		
None	0	25/25 (100%)
Single	1	0/25 (0%)
Multiple	2	0/25 (0%)
Trunk/Breast		
None	0	25/25 (100%)
Single	1	0/25 (0%)
Multiple	2	0/25 (0%)

See Table 12 for the mean cord number scores of the participants.

Table 3. Variation in Cord Thickness by Anatomical Locations

Anatomical locations	Cord thickness scores (0-3)	Number and percentage of participants
Axilla		
None	0	0/25 (0%)
Fine	1	0/25 (0%)
Thin	2	3/25 (12%)
Thick	3	22/25 (88%)
Upper Arm		
None	0	0/25 (0%)
Fine	1	0/25 (0%)
Thin	2	3/25 (12%)
Thick	3	22/25 (88%)
Elbow		
None	0	17/25 (68%)
Fine	1	0/25 (0%)
Thin	2	8/25 (32%)
Forearm		
None	0	20/25 (8%)
Fine	1	0/25 (0%)
Thin	2	3/25 (12%)
Thick	3	2/25 (8%)
Wrist		
None	0	25/25 (100%)
Fine	1	0/25 (0%)
Thin	2	0/25 (0%)
Hand/Fingers		
None	0	25/25 (100%)
Fine	1	0/25 (0%)
Thin	2	0/25 (0%)
Trunk/Breast		
None	0	25/25 (100%)
Fine	1	0/25 (0%)
Thin	2	0/25 (0%)
Thick	3	0/25 (0%)

See Table 12 for the mean cord thickness scores of the participants.

Table 4. Variation in Cord Depth by Anatomical Locations

Anatomical locations	Cord depth scores	Number and percentage of participants
Axilla		
None	0	0/25 (0%)
Superficial	1	0/25 (0%)
Intermediate	2	7/25 (28%)
Deep	3	18/25 (72%)
Upper Arm		
None	0	0/25 (0%)
Superficial	1	0/25 (0%)
Intermediate	2	7/25 (28%)
Deep	3	18/25 (72%)
Elbow		
None	0	16/25 (64%)
Superficial	1	1/25 (4%)
Intermediate	2	8/25 (32%)
Forearm		
None	0	20/25 (80%)
Superficial	1	0/25 (0%)
Intermediate	2	5/25 (20%)
Deep	3	0/25 (0%)
Wrist		
None	0	25/25 (100%)
Superficial	1	0/25 (0%)
Hand/Fingers		
None	0	25/25 (100%)
Superficial	1	0/25 (0%)
Trunk/Breast		
None	0	25/25 (100%)
Superficial	1	0/25 (0%)
Intermediate	2	0/25 (0%)

See Table 12 for the mean cord depth scores of the participants.

Table 5. Presence of Swelling by Anatomical Locations

Anatomical locations	Regional swelling scores (0-1)	Number and percentage of Participants
Axilla		
None	0	13/25 (52%)
Present	1	12/25 (48%)
Upper Arm		
None	0	8/25 (32%)
Present	1	17/25 (68%)
Elbow		
None	0	10/25 (40%)
Present	1	15/25 (60%)
Forearm		
None	0	11/25 (44%)
Present	1	14/25 (56%)
Wrist		
None	0	14/25 (56%)
Present	1	11/25 (44%)
Hand/Fingers		
None	0	18/25 (72%)
Present	1	7/25 (28%)
Trunk/Breast		
None	0	22/25 (88%)
Present	1	3/25 (12%)

See Table 12 for the mean cord swelling scores of the participants.

Table 6. Distribution of Range of Motion Restriction in Shoulder Abduction

Range of motion	Range of scores (0-10)	Number and percentage of participants
170-180	0	11/25 (44%)
150-170	1	7/25 (28%)
120-150	4	5/25 (20%)
90-120	7	2/25 (8%)
<90	10	0/25 (0%)

See Table 12 for the mean shoulder abduction restriction scores of the participants.

Table 7. Distribution of Range of Motion in Shoulder Flexion Restriction

Range of motion	Range of scores (0-10)	Number and percentage of participants
170-180	0	10/25 (40%)
150-170	1	10/25 (40%)
120-150	4	3/25 (12%)
90-120	7	2/25 (8%)
<-90	10	0/25 (0%)

See Table 12 for the mean shoulder flexion restriction scores of the participants.

Table 8. Distribution of Range of Motion in Elbow Extension Restriction

Elbow extension restriction	Range of scores (0-3)	Number and percentage of participants
None	0	24/25 (96%)
Mild	1	0/25 (0%)
Moderate	2	1/25 (4%)
Severe	3	0/25 (0%)

See Table 12 for the mean elbow extension restriction scores of the participants.

Table 9. Distribution of Range of Motion in Hand and Wrist Restriction

Hand and wrist restriction	Range of scores (0-3)	Number and percentage of participants
None	0	22/25 (88%)
Mild	1	2/25 (8%)
Moderate	2	1/25 (4%)
Severe	3	0/25 (0%)

See Table 12 for the mean hand/wrist restriction scores of the participants.

Table 10. Distribution of Pain Scores

Pain VAS	Range of scores (0-10)	Number and percentage of participants
None	0	13/25 (52%)
Mild pain	1-3	3/25 (12%)
Moderate pain	4-7	9/25 (36%)
Severe pain	8-10	0/25 (0%)

Table 11. Distribution of ADL Limitation Impact Scores

ADL limitation impact	Range of scores (0-10)	Number and percentage of participants
None	0	12/25 (48%)
Mild impact	2	9/25 (36%)
Moderate impact	6	4/25 (16%)
Severe impact	10	0/25 (0%)

See Table 12 for the mean ADL scores of the participants.

Table 12: Total Scores for All AWS Criteria

AWS scoring criteria	Maximum scores	Mean scores (SD) of participants	Percentage of maximum scores
Morphological descriptors			
Number	14	3.60 (1.63)	26%
Thickness	18	6.88 (2.07)	38%
Depth	15	6.52 (2.06)	43%
Swelling	7	3.20 (2.65)	46%
Pain	10	2.08 (2.33)	21%
Functional descriptors			
Shoulder Abduction	10	1.64 (2.22)	16%
Shoulder Flexion	10	1.44 (2.08)	14%
Elbow Extension	3	0.08 (0.40)	3%
Hand/Wrist	3	0.16 (0.47)	5%
ADL Limitations	10	1.68 (2.14)	17%
Total	100	27.20 (10.05)	

The maximum scores represent the sum total of all anatomical location scores (e.g. axilla, upper arm, elbow, forearm, wrist, hand/fingers, trunk/breast) for each AWS scoring criteria. The percent of maximum score for each criterion is calculated by the mean score divided by the maximum score.

Table 13: Distribution of AWS Severity Scores

Category levels of AWS severity	Range of severity scores (pts)	Actual mean (SD) severity scores	Number and percentage of participants
Very mild	1-5	0 (0)	0/25 (0%)
Mild	6-25	18.50 (3.61)	12/25 (48%)
Moderate	26-50	33.92 (4.91)	12/25 (48%)
Severe	>51	51	1/25 (4%)

Range of scores is determined from the sum of scores of the morphological measures (e.g. number, thickness, depth, and swelling of cords), pain (VAS scale), upper extremity ROM and restrictions, and ADL limitations. Actual mean scores were calculated by dividing the sum of the points in each category level of AWS by the number of participants in each category level.

Morphological summary

The morphological component provided information on cord integrity and the areas of importance. Cording was primarily concentrated in the axilla and upper arm. The greatest number of cords was observed in these areas (Table 2). The cording in these areas was the thickest and deepest, with cords thinning out and becoming less deep distally in the arm (Tables 3 and 4). Finally, swelling was less isolated, extending all the way into the hands and fingers for some of the participants, concentrated throughout the axilla into the forearm (Table 5).

Functional summary

The functional component focused on the restrictions in range of motion in different parts of the arm. Around half of the participants experienced little to no restrictions when performing shoulder abduction, with the most severe cases not diminishing to less than 90° throughout the movement (Table 6). Shoulder flexion was slightly more compromised, with over half of the participants unable to lift their arms fully above the head (Table 7). The majority of participants did not see any changes in elbow extension or hand and wrist movement (Tables 8 and 9).

Pain summary

Pain related to cording in AWS was varied throughout the participants. Over half of the women gave a score of 0 on the visual analog scale. The highest level of pain did not exceed a 5 on the scale, with the second largest group in this category describing moderate levels of pain (Table 10).

QuickDASH scoring and relationships

The average score on the QuickDASH for the 25 participants was 29.8 (SD=19.7) with a range of scores from 0 to 72.7. The relationship between AWS severity score and QuickDASH score was assessed using a Pearson correlation. Results revealed a moderate to strong positive correlation, $r=0.65$ ($p<0.001$), indicating that a higher AWS severity score is associated with a higher QuickDASH score (Figure 1).

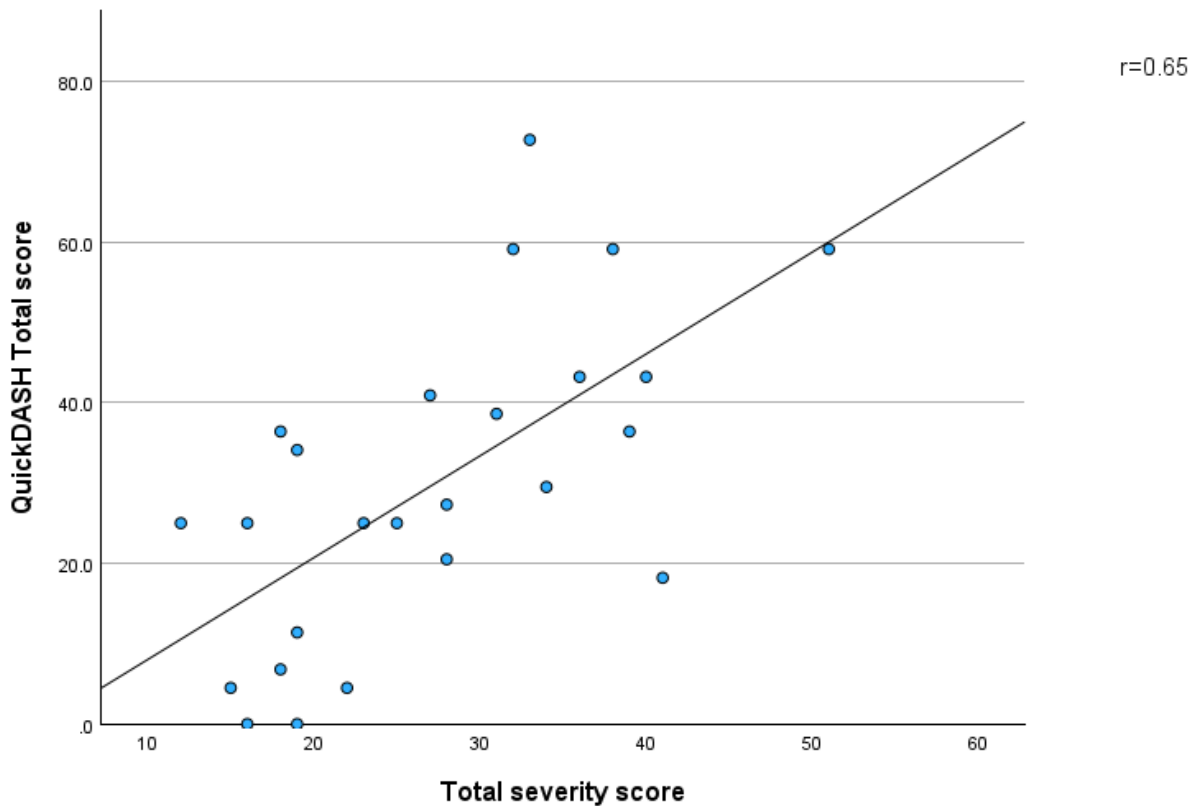


Figure 1: Relationship between Total Severity Score and Total QuickDASH Score in AWS

An independent samples t-test was performed to examine the severity score between the participants that presented with pain and those that did not. The presence of pain was defined as having a non-zero score on the VAS pain scale on the AWS severity scoring sheet. The results showed a significant difference in scores, $t = 4.347$, $p<0.001$. Participants that presented with pain ($n=12$) had significantly higher AWS severity scores (mean=34.08, SD=8.31) compared to

those without pain (n=13) (mean=20.85, SD=6.90). The mean difference in scores was 13.24 (95% CI: 6.94, 19.54), with a large effect size (Cohen's d=1.740), which would suggest that there is a large important difference between the two groups (Figure 2).

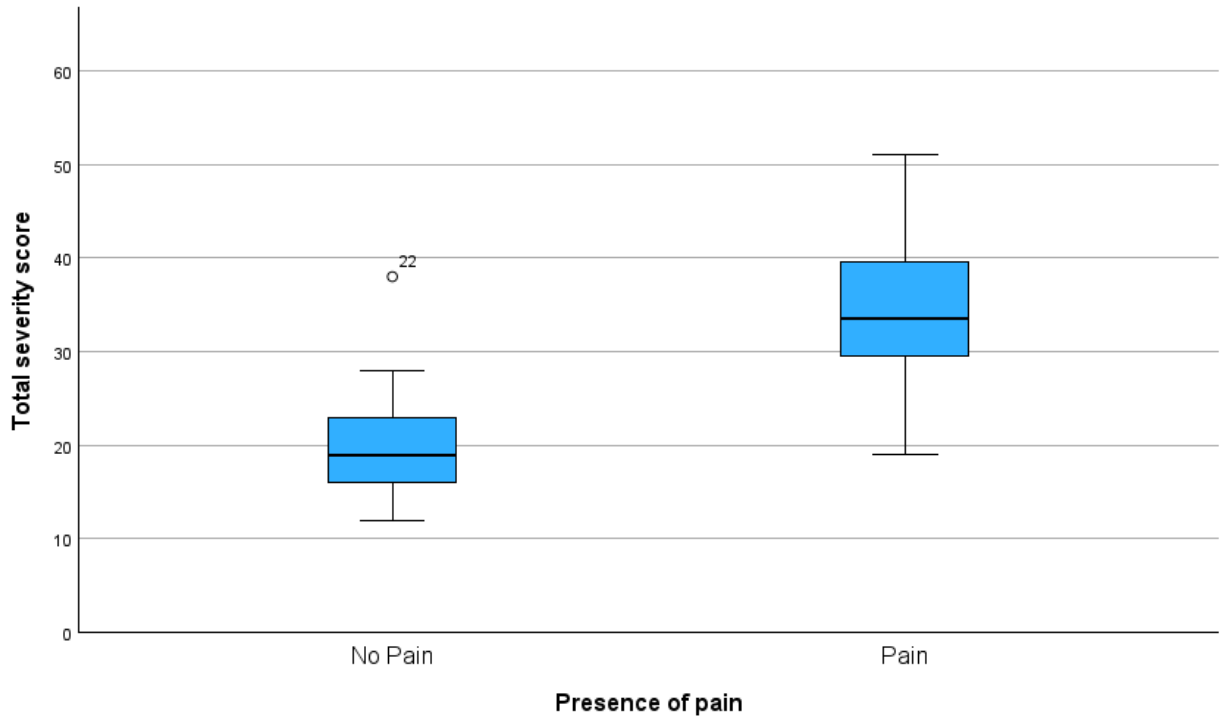


Figure 2: Total Severity Score Differences in Individuals with and without Pain

Given the significant role of pain in AWS, further analysis on this measure was conducted using a Pearson correlation examining the relationship between the VAS pain scale on the AWS severity scoring sheet and the “pain” subset in the QuickDASH questionnaire, or the sum of the scores for questions 9 and 10. Results from this analysis demonstrated a moderately positive correlation ($r=0.52$, $p=0.008$), suggesting that higher scores on the VAS pain score on the AWS severity scoring sheet are associated with higher scores in the “pain” subset of the QuickDASH (Figure 3).

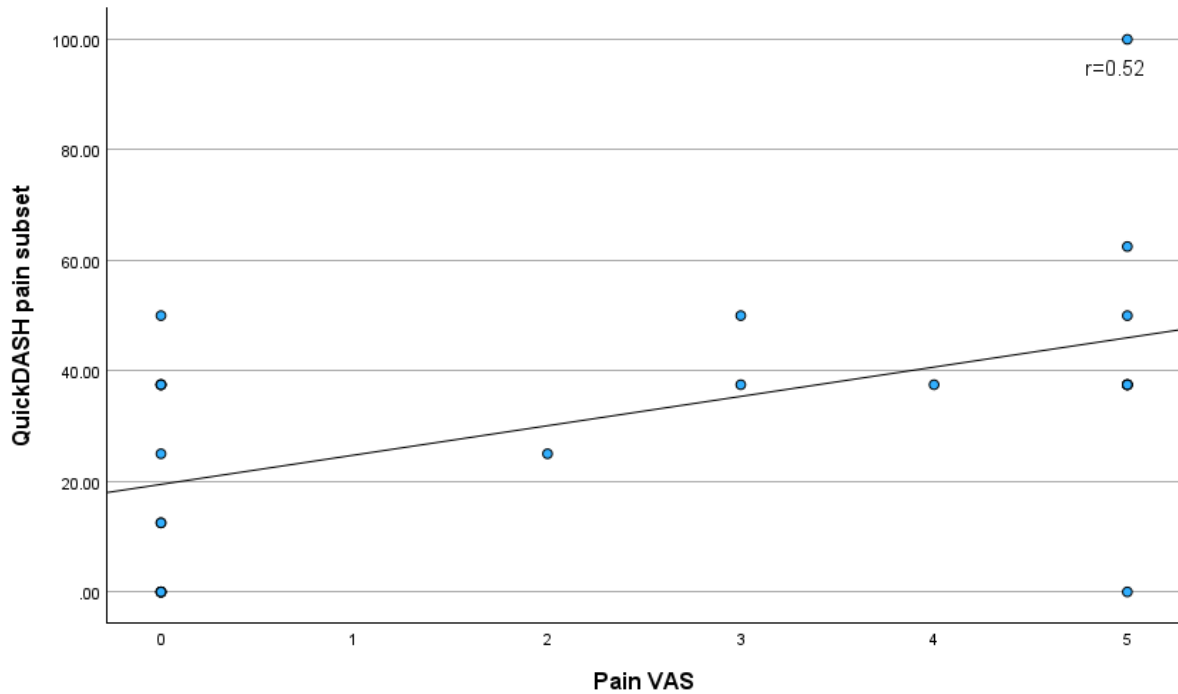


Figure 3: Relationship between Pain VAS and QuickDASH Pain Subset Scores

An initial analysis comparing AWS severity scores between participants who underwent ALND and those that had undergone SLNB was suggested. Due to most participants being in the ALND group, a comparison with the SLNB group was not practical. A Pearson correlation was therefore conducted to observe the relationship between severity scores and the total number of lymph nodes removed during axilla surgery. The results showed a non-significant, weak association between these two variables ($r=0.29$, $p=0.264$), suggesting that within this sample ($n=17$), the number of lymph nodes removed was not strongly correlated to total AWS severity scores.

A Pearson correlation analysis was conducted to assess the relationship between BMI and AWS severity scores. Results showed a weak non-significant correlation ($r=0.31$, $p=0.133$), indicating that BMI may not be a factor contributing to the severity scoring of AWS.

An analysis between the lymphedema and non-lymphedema groups was performed to assess any difference in measures: independent sample t-tests between each group were conducted on variables of interest, including total AWS severity scores and the associated subsections, QuickDASH scores and BMI. Results yielded no significant differences between groups.

Discussion

The purpose of this study was threefold. First, a novel scoring system for AWS was introduced to measure specific characteristics contributing to the severity of the condition. These characteristics included anatomical (size and depth) and positional (location) variables as well as range of motion limitations in the shoulder, elbow, wrist and hand. A severity score for AWS was then obtained through the sum of all these characteristics. The second aim was to investigate the relationship between AWS severity, obtained from the novel scoring system, and physical function, determined using the QuickDASH questionnaire scores. Finally, the third aim was to observe any correlation between the presence of pain and determine if there was any impact on AWS severity scores.

Addressing the first aim, the presence of cording was primarily condensed in the axilla and upper arm, with the greatest number and thickness of cords seen proximally, decreasing in number and size distally. Previous studies have identified similar locations for cord distribution, beginning in the axilla and extending towards the hand (Koehler et al., 2018). This concentration of cording in these regions of the upper limb can significantly affect arm function: a previous study by Koehler et al. (2015) describes lower ranges of motion in shoulder abduction and flexion in participants with AWS when compared to women who did not develop AWS following breast cancer surgery. McNeely et al. also identified shoulder abduction and flexion as variables of interest, with shoulder abduction showing greater restrictions than shoulder flexion (2024); the results in the current study coincide with these findings. However, in the present study, only 56% (n=14) and 60% (n=15) of participants presented with minimal to mild restrictions in shoulder abduction and shoulder extension, respectfully. While range of motion may be a compromising factor in AWS, it would appear that in the present study, isolated joint mobility was not

significantly impacted. The location of the axillary lymph nodes and vessels concentrated in the anterior axilla can affect movement in the shoulder joint, especially if the arm is raised above the shoulder, leading to increased stretching in anterior axillary region (Soares, 2014). Fibrosis of lymphatic tissue in this region can lead to compromised arm movements such as shoulder abduction and flexion, as mentioned in the previous study by Koehler et al. (2018) and seen in certain women in the current study. Hypothetically, an increased number of cords would signify larger amounts of fibrotic scar tissue, creating more tension and increasing difficulty when performing upper limb movements. However, in the present study, no significant correlation was observed between the number of cords and restrictions in shoulder movement, possibly due to the small sample size or the way that the “number of cords” variable was categorized. In the scoring system, “multiple cords” was categorized as one group, without any further distinction (i.e. 2 cords vs 5 cords). This may potentially mask differences with varying numbers of cording and severity. Movement in AWS may be restricted due to the mechanical stretching of the scar tissue, which can cause sensations of tightness and pulling. Since the cords are believed to be scarred lymphatic vessels, they are likely tethered to surrounding tissue, notably the deeper layers of the skin. Superficial lymphatic vessels are located in the dermis: these vessels are smaller, comprised of capillaries and pre-collectors that direct the lymph towards lymph-collecting vessels. These larger lymph-collecting vessels are present in the subcutaneous tissue and collect lymph from the smaller vessels to be redirected towards the lymph nodes (Suami & Scaglioni, 2018). In the present study, 88% of participants (n=22) presented with thick cords in the axilla region, and 72% of participants (n=18) experienced cording deep in the axilla. These findings suggest that the primary lymphatic structures affected in AWS are the larger and deeper vessels in the axilla. Regardless of the layer in which they are located in, lymphatic vessels are

primarily anchored to fascia, otherwise known as connective tissue surrounding muscles and other soft structures (Varghese & Priya, 2017). Fibrosis and scarring of lymphatic vessels may therefore result in tightness and pulling of the fascia, leading to the hallmark symptoms of restrictions in range of motion and pain.

Regional or localized pain has been reported in women with AWS in association with fibrotic lesions causing tightness of the vessel (Dinas et al., 2019). In the present study, around half of the participants, or 48% (n=12), experienced pain at rest or during ROM measurements. Analysis of the results revealed no direct link between the severity of AWS or the accumulation of scores from the morphological, and functional measures obtained and the rating of pain on the VAS pain scale. For example, participants who reported a non-zero score on the VAS pain scale obtained significantly higher AWS severity scores compared to those who experienced no pain. This suggests that there may be a threshold effect where the presence of pain, regardless of the magnitude, may indicate an increase in cording severity. Furthermore, the subjectivity of pain can vary among participants, influenced by factors such as increased pain tolerance after prolonged exposure, or pain habituation (van der Miesen et al., 2024). Previous research has shown that individuals' self-perceived pain sensitivity does not appear to be linked to laboratory measured responses to standardized noxious stimuli (Edwards & Fillingim, 2007). This may lead to variations in scores that may not reflect the actual severity of AWS. Data from the current research shows that the degree of severity of pain seems to have minimal impact on overall AWS severity scores. Thus, a binary classification of pain, such as "present vs absent" may be a more appropriate way to represent pain for the current AWS scoring tool. Ultimately, this will simplify data collection and reduce subjectivity.

The current results showed a significant positive correlation between AWS severity scores and QuickDASH scores, indicating that increased cord severity is associated with a higher QuickDASH score, or decrease in upper-limb function. These findings are consistent with previous research concerning the common symptoms of AWS, which list restrictions in range of motion and pain as notable complications (Koehler et al, 2018). The QuickDASH has been proven to be a reliable and valid instrument in measuring upper extremity disability in breast cancer survivors, so the positive correlation between this tool and AWS severity highlights the potential usefulness of the AWS scoring system in postoperative assessments. This finding further highlights the significance of physical function in AWS by using a validated tool to measure functional outcomes. The current results are consistent with previous literature surrounding AWS' negative impact on function in the shoulder and arm, with reductions in range of motion and difficulties with the performance of daily activities (Yeung et al., 2015). While the current study did not find any significant impact of AWS severity on specific joint range of motions such as shoulder flexion and abduction, a significant association between AWS severity and general upper limb function was identified, as highlighted by the elevated QuickDASH scores in participants with higher severity scores. This suggests that the impacts of AWS are broader than solely single plane movements and that functional limitations arise when patients perform a series of movements requiring a sequence of multi-plane actions.

A previous study by Koehler et al. (2015) has highlighted a link between BMI and AWS, identifying a higher incidence rate of AWS in patients with lower BMI. Based on this, we had hypothesized that participants with a lower BMI would present with increased AWS severity. However, the current study did not establish a significant relationship between these two factors: the severity of AWS was not significantly associated with a lower BMI. A possible explanation

for this discrepancy is that the identification of cording may be more difficult in patients with more subcutaneous adipose tissue. You-Ten et al. (2015) found that palpation inaccuracies were greater in obese versus non-obese women. Palpating for cords in women with a lower BMI may yield more accurate results since cording is more easily discernable at lower BMIs. This shows a potential detection bias, which could lead to an underestimation of the severity of AWS in patients with a higher BMI. Further research must be done on the integrity of AWS cording so that clinicians can identify more accurate ways to examine cords.

The type of axilla surgery performed during breast cancer treatment was hypothesized to be a factor that may contribute to the severity of AWS. Surgery complexity has been highlighted as a risk factor for the development of AWS since more invasive surgeries further compromise lymphatic function: increased number of lymph nodes removed negatively impacts lymph movement in the limbs (Yeung et al., 2015). Our results did not show any significant relationship between surgery types (ALND vs. SLNB) and AWS severity. A larger number of removed lymph nodes was not associated with an increase in AWS severity. Participant medical history on the specific number of removed lymph nodes was only available for 17 out of the 25 women, so this smaller sample size may potentially limit the statistical power to detect any significant relationship between these factors.

Alongside lymph node removal, another variable of interest was the presence of lymphedema and its impact on AWS. Lymphedema and AWS are both closely linked to disruptions of the lymphatic system. Our original hypothesis of an increase in AWS severity with the presence of lymphedema was not supported by the current results. While the distribution of the groups in our study was uneven, with only five out of the 25 women, or 20%, presenting with lymphedema, our analysis showed no significant difference in severity between women with and

without lymphedema. Previous research has identified the development of AWS earlier on the postoperative timeline, typically several weeks following surgery, while lymphedema was identified several months after surgery (Koehler et al., 2018). Given the uncertainty of when each complication develops on the timeline, categorizing AWS or lymphedema as a risk factor for one another may not be entirely accurate. While they are both conditions that are closely related, it may be wiser to treat them as comorbidities rather than risk factors for each other.

Conclusion

AWS is an emerging complication following breast cancer surgery that can compromise physical function and impact activities of daily living. Despite its increasing clinical relevance, limited research and knowledge on cording morphology and specific disease impacts on physical function make it difficult for healthcare professionals to adequately assess the condition. The current assessment method is only determined by the presence or absence of cording, with limited consideration of severity and subsequent impact on function. Developing a reliable method to quantify the severity of AWS would allow for the stratification of severity, which would enable personalized interventions and ultimately improve patient outcomes. Based upon the criteria used in the present study, the AWS severity scoring system can be used to assess the decline in physical functioning of women with AWS.

The current findings of this study indicate that AWS cording appears to be concentrated in the axilla and upper arm, with the largest and deepest cords being identified in those locations: this suggests that larger and deeper lymphatic vessels seem to be primarily affected in AWS. Furthermore, the compromised ranges of motion seem to be predominantly multi-jointed movements rather than single-jointed. Finally, pain, specifically its presence rather than its magnitude, appear to play a significant role in AWS severity.

Limitations

The findings from the current study provide further insight into the impacting factors of AWS, as well as variables of interest that may affect the severity of the condition. However, several factors should be considered when interpreting the results of this study, some of which have been briefly discussed above. The relatively small sample size of 25 participants may have reduced the statistical power of the analysis, possibly masking any meaningful findings. The

homogeneity of the sample size was also a notable restriction: all of the participants were recruited from an existing group of patients at a clinic with a similar demographic, notably older women with an elevated BMI. The possibility of analyzing subgroups was therefore restricted, as seen when analyzing certain factors such as BMI and the presence of lymphedema and their impact on AWS. The small sample size may also be associated with a lack of distribution of the results: the majority of participants fell into two categories of severity (mild or moderate), with only a singular participant evaluated as severe and none as very mild. The categorization of certain elements on the AWS severity grading tool could also have limited the significance of certain findings, particularly the variable pertaining to the number of cords, which did not specify a number of cords, but rather a broad category (see appendix 1). Cording morphology was done by visual inspection and palpation, performed by one consistent evaluator; any measurement error would therefore be consistent. Finally, the reliance on a self-reported questionnaire such as the QuickDASH may have been a limitation, since it is subject to personal interpretation. Particularly, some participants expressed difficulty answering certain questions when the arm affected by AWS was not their dominant arm. Certain items on the questionnaire, such as opening a jar or using a knife, are most commonly performed using the dominant arm; this may lead to an added element of variability in participant perception and reported functional limitations.

Future Directions

A companion study assessing the reliability of the AWS grading tool is currently under way, which will shed light on inter-rater and intra-rater reliability to allow for further clinical use. Future research should focus on examining the structure and composition of the cording seen in AWS to precisely identify the cause behind the development of these cords. A study with a larger

sample size composed of a more diverse variety of participants with different demographic characteristics may be of interest to detect any potential risk factors that may impact the severity of AWS. Based on the results drawn from the current study, certain modifications to the AWS severity scoring system could be made to allow for a more robust assessment; potential changes could include a different grading of pain (binary vs the current scale) or a more extensive section on impacts of activities of daily living at the expense of a less detailed range of motion portion. Finally, additional longitudinal studies would be beneficial to further observe disease progression, potential long-term effects and the impact and effectiveness of specific treatment interventions.

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Appendix B – QuickDASH Questionnaire

THE **QuickDASH**

OUTCOME MEASURE

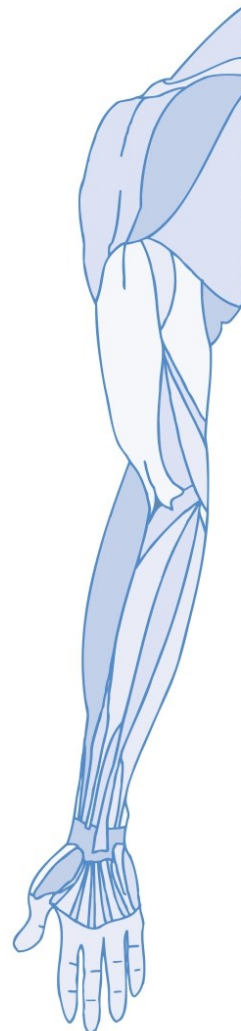
INSTRUCTIONS

This questionnaire asks about your symptoms as well as your ability to perform certain activities.

Please answer *every question*, based on your condition in the last week, by circling the appropriate number.

If you did not have the opportunity to perform an activity in the past week, please make your *best estimate* of which response would be the most accurate.

It doesn't matter which hand or arm you use to perform the activity; please answer based on your ability regardless of how you perform the task.



QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, to what extent has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. (circle number)

	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? (circle number)	1	2	3	4	5

QuickDASH DISABILITY/SYMPTOM SCORE = $\left(\left[\frac{\text{sum of } n \text{ responses}}{n} \right] - 1 \right) \times 25$, where n is equal to the number of completed responses.

A QuickDASH score may not be calculated if there is greater than 1 missing item.