Ann. Cancer Res. Ther. Vol. 32, No. 2, pp. 45-55, 2024

Review Article

Comparative Effectiveness of Adjunct Therapies and Exercise Versus Exercise Alone in Managing Axillary Web Syndrome following Breast Cancer Surgery: A Systematic Review

Julia Janina Chojnacka[1)], Adebayo Omileye[2)], Gebrye Tadesse[1)], Francis Fatoye[1)], Chidozie Mbada[1)]

[1)] *Department of Health Professions, Faculty of Health and Education, Manchester Metropolitan University, Birley Fields Campus, Manchester, United Kingdom*
[2)] *Department of Medical Rehabilitation, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria*

Abstract

Introduction: Axillary web syndrome (AWS) continues to be a misunderstood and poorly researched sequela of Breast Cancer (BC) care. Attempts have been made to encapsulate the optimal rehabilitative approach. This systematic review (SR) examines the effectiveness of adjunct therapies combined with Exercise-Based Interventions (EBIs) versus EBIs alone in managing AWS following BC surgery.
Methods: Following the PRISMA guidelines for SRs, PubMed, Scopus, EBSCO CINAHL, EBSCO Medline, and Cochrane CENTRAL were systematically searched for eligible studies on the effectiveness of EBIs or any adjunctive intervention for AWS in terms of pain, health-related Quality of life (HRQoL) and resolution of AWS. The JBI critical appraisal guide for SR was used to assess the quality of eligible studies.
Results: The search yielded 1302 records. Six studies were included in this review. The EBIs consisted of active, passive, and active-assisted stretching, mobility exercises, proprioceptive neuromuscular facilitation, and progressive functional activities. Other therapies included soft tissue mobilisations (STM), manual lymphatic drainage (MLD), myofascial release, and vacuum-sealing drainage. EBIs were significantly beneficial in resolving AWS (in two studies), preventing AWS (in one study), reducing AWS-related pain (in four studies), and improving HRQoL (in three studies). Exercise was often prescribed with STM in the axilla of the operated side. Significantly greater effects were observed in all three outcomes when EBIs were recommended with MLD.
Conclusion: EBIs are effective in treating AWS and its associated symptoms. However, the prescription of exercise therapies with MLD appears to be superior in treating symptoms, resolving AWS quicker, and preventing its development.

Keywords: Axillary Web Syndrome, Breast Cancer, Exercise-based Interventions, Management, Physiotherapy

(Received July 19, 2024; Accepted October 15, 2024)

Introduction

Breast cancer (BC) is the most common cancer among women in the UK, with over 55,000 new cases annually[1)]. Surgery and axillary dissection are crucial for prognosis and preventing metastasis or recurrence[2)]. Depending on tumour severity, either a sentinel lymph node biopsy (SLNB) or a full axillary lymph node dissection (ALND) is performed[3)]. SLNBs are preferred due to fewer post-operative complications[4, 5)]. Disruption in the axillary lymphatic system can lead to short-term and long-term complications, such as pain[6, 7)], neuropathic sensations[8, 9)], reduced shoulder range of motion (ROM)[10)], seroma[11)], and rarely lymphoedema[12)]. In addition, these issues negatively impact health-related quality of life (HRQoL)[13, 14)].

Corresponding author: Dr. Chidozie Emmanuel Mbada, Department of Health Professions, Faculty of Health and Education, Manchester Metropolitan University, Birley Fields Campus, Manchester, M15 6GX, United Kingdom. E-mail: c.mbada@mmu.ac.uk, TEL: +44 161 247 2936

A significant complication following BC surgery is axillary web syndrome (AWS)[15-17)]. AWS, or cording, was coined by Moskovitz et al.[18)] and is characterised by a visible, palpable cord in the axilla of the arm on the same side as the breast surgery, especially noticeable with shoulder abduction. The cord extends down the medial side of the arm to the antecubital fossa and sometimes to the wrist[19)]. Patients with AWS experience limited range of motion (ROM), a pulling sensation, tightness, and a dull ache or pain with elbow extension, shoulder abduction, or flexion[20)]. Current literature is yet to agree on the aetiology of AWS, however, it is associated with disruptions to the lymphatic vessels. During surgery, venous clipping and resection can disrupt the movement of the lymph fluid, causing lymphatic stasis, inflammation, and fibrosis[21)]. Disruptions to the lymphatics cause a state of hypercoagulation of the surrounding tissues[22)], reducing the extensibility of lymph vessels[23)]. This indicates a potential justification for why AWS appears cord-like and is palpable directly over damaged lymphatic vessels.

Although AWS is recognised as a niche area of BC care, physiotherapists worldwide often encounter this issue in practice. Koehler et al.[24] estimated an incidence rate of 6–86% for AWS, emphasizing the need for thorough examination by healthcare professionals. Bergmann et al.[25] and Torres Lacomba et al.[26] reported incidence rates of 28.1% and 48.3%, respectively. Prevalence rates vary due to differing definitions and diagnostic criteria[27, 28]. AWS is 1.7–7 times more prevalent following ALND than SLNB[27]. Other risk factors include younger age[29], lower body mass index[30], and extensive oncological treatments like mastectomy, ALND, and chemotherapy[28].

AWS typically appears within the first eight weeks post-surgery[31], though recent research suggests onset can occur within the first few months[32]. While early studies indicated AWS might resolve spontaneously within 3–4 months[4, 18], contemporary research shows it can persist up to 18 months post-surgery[33]. This highlights the need for therapeutic intervention to address this long-term complication. Ibrahim et al.[34] noted that AWS complications can lead to poor posture, shoulder impingements, movement restrictions, or chronic pain. Addressing AWS is crucial, as additional therapies like radiotherapy or chemotherapy can increase the risk of AWS or recurrence[26].

There is no consensus on the best approach to managing AWS. The National Institute for Health and Care Excellence (NICE) guidelines for post-breast cancer surgery management do not include AWS, recommending only general functional exercises[35]. Many studies advocate physiotherapy for AWS[16, 24, 36, 37], but McNeely et al.[38] caution that early post-operative exercises can cause seromas, bleeding, and delayed healing. High-quality studies using randomised controlled trials (RCT) are needed to verify findings and agree on effective physiotherapy modalities[31]. Dinas et al.[21] recommend active-assisted and passive range of motion (ROM) exercises, soft tissue mobilisations (STM), and manual lymphatic drainage (MLD). Lippi et al.[14] found that exercise and manual therapy (MT) are most effective for AWS resolution and pain reduction, compared to other treatments like moist heat, compression, plant-based medicaments, or aqua lymphatic therapy. However, their review was based on low-quality evidence, mainly case reports. The findings emphasised the need for comparative data between the treatment options. Therefore, this systematic review aimed to investigate the effectiveness of adjunct therapies used alongside exercise-based interventions versus exercise-based interventions alone in the management of AWS in terms of resolution or prevention of AWS, pain, and HRQoL.

Materials and Methods

Introduction

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[39]. This review was registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/PROSPERO - CRD42024596403.

Eligibility Criteria

To ensure a comprehensive selection of studies, the Population, Intervention, Comparison, and Outcomes (PICO) model was used to establish an appropriate eligibility criterion[40]. Using the PICO model, the eligibility criteria for the study was determined as shown in Table 1. Due to the urgent appeal within the literature for more high-quality evidence to be used, this review excludes case reports, case series or other descriptive studies and only includes studies that were registered after January 2012. The full eligibility criteria are outlined in Table 2 below.

Search Strategy

The data search was completed through a thorough and systematic investigation of five electronic databases, commonly used for physiotherapy and oncology research. PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EBSCOhost MEDLINE, EBSCO CINAHL (Cumulative Index to Nursing and Allied Health Literature) and Scopus were searched between January 2012 and March 2023. No restrictions were applied for publication origin, keywords, or types of research design. The search analysed titles, abstracts and keywords using MeSH (Medical Subject Headings) terms focused on the key terms 'breast cancer', 'Axillary Web

Table 1 PICO Model

PICO	Criteria
Population	BC patients who were 18+ years of age, who had undergone a lumpectomy, mastectomy or quadrantectomy and had an axillary lymph node surgery, either SLNB or ALND, with a clinical diagnosis of AWS.
Intervention	Exercise-based interventions plus other physiotherapeutic techniques/modalities (manual lymphatic drainage, myofascial release (MFR), manual therapy, Light Amplification by Stimulated Emission of Radiation (LASER), Soft Tissue Mobilisation (STM)).
Comparison	Exercise-based interventions (Exercises, Active and Passive Stretching, Active and Passive Range of Movement Exercise (Shoulder and Upper Limb) plus STM/education
Outcomes	AWS resolution or prevention, pain, and quality of life.

Table 2 Eligibility Criteria

Inclusion	Exclusion
• Studies conducted and published after January 2012 • Any experimental research (e.g RCTs, non-RCTs, quasi-experiments or clinical trials) • Observational studies or pilot studies which follow PICO • Adult male or females with a history of breast cancer and tumour-removing surgery • Any therapeutic or physiotherapist- prescribed rehabilitative modality • Studies addressing treatment options for AWS • Manuscripts available in English or available to translate into English	• Descriptive studies or articles, e.g case reports, series or qualitative • Other research designs, e.g editorials, letters, comments, consensus statements • Reviews, e.g systematic, meta-analysis, literature review • Interventions outside of PICO, e.g drug medications, surgical manipulations of the cords or invasive approaches • Study including participants with recurrence or previous shoulder pathologies • Studies focusing on incidence alone without a physical intervention • Mondor's disease or AWS present in participants without breast cancer • Studies involving animals • Texts not available in the English language • Unavailable full-text manuscripts

Table 3 Search Strategy

PubMed:
("Axillary Web Syndrome" OR AWS OR Cording OR Lymphatic cording OR lymphatic fibrosis OR Axillary cord OR Axillary band) AND (Breast cancer OR "Breast malignancy" OR "breast tumour" OR "breast neoplasm" OR Mastectomy OR lumpectomy) AND (treatment OR physical therap* OR "physical treatment" OR exercise OR therapeutic treatment OR "therapeutic exercis*" OR stretch* OR "active stretch*" OR "passive stretch*" OR "physiotherapy treatment" OR "physiotherapy manage*" OR rehabilitation OR "soft tissue mobilis*" OR massage OR "cord* mobilis*")
Other Databases:
("Axillary Web Syndrome" OR AWS OR Cording OR "Lymphatic cording" OR "Lymphatic fibrosis" OR "Axillary cording" OR "Axillary cord*" OR "Axillary band") AND (Breast cancer OR "Breast malignancy" OR "breast tumour" OR "Breast neoplasm" OR "Mastectomy" OR "lumpectomy") AND (Treatment OR Physical therap* OR "Physical treatment" OR Exercise OR "Therapeutic treatment" OR "Therapeutic exercis*" OR stretching Or "Active stretch*" Or "Passive stretch*" or "physiotherapy treatment" Or "Physiotherapy manage*" OR rehabilitation Or "soft tissue mobilis*" Or "massage" Or "Cord* mobilis*")

Syndrome' and 'Physiotherapy'. All databases followed the same search strategy except PubMed which removed "Axillary cording" and changed "stretching" to "stretch*". The full search strategy is displayed in Table 3. The results of the searches were exported through citation manager to a reference management software Endnote v. 20[41], where they were screened for eligibility.

Selection Process

The screening process was completed by one independent researcher. Despite single viewer screening posing a risk for researcher bias[42], this methodological adjustment from recommended standards of reviews was put into effect due to the purpose of this review and academic regulations. Prior to screening, EndNote v. 20[41] was used to identify and remove duplicates from the search list. The researcher then manually examined the results to identify and eliminate any duplicates the software overlooked. This was done by sorting the reports into ascending alphabetical order according to study titles and identifying any titles that appeared more than once. The titles and abstracts of the reports were then screened to establish studies that adhered to PICO. Manuscripts that complied with the PICO framework for this review were sought for retrieval to obtain full text reports. The remaining reports were then screened for eligibility of the inclusion and exclusion criteria and included in the review.

Data Extraction

Data extraction was conducted manually by an independent researcher and imported manually into Excel document for organisation. The subsequent data was extracted from each study: 1) study title 2) lead author 3) year of publication 4) country of publication 5) study design 6) participant characteristics 6) description of intervention 7) description of control group 8) outcome measures used and 9) key relevant findings. The extracted data are presented in Table 4. The outcomes of each study related to pain, resolution of AWS and HRQoL were extracted and summarised separately in preparation for analysis.

Quality Assessment

To ensure quality of evidence, the six RCTs used in this review were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal tool for Assessment of Risk of Bias for Randomised Controlled Trials[43]. The tool includes 13-questions assessing the risk of bias (RoB) based on selection, allocation, administration of intervention, assessment, measurements of the outcome, participant retention and statistical conclusion validity on a 'yes', 'no', 'unclear', or 'not applicable' response basis. Current literature supports the use of the JBI critical appraisal tools as an appropriate tool to assess RoB in systematic review[44-46].

Table 4 Main characteristics of the included studies

Study	Study design	Participants	Intervention	Control	Outcomes
Cho et al., 2016 (50) **South Korea**	RCT	48 participants: 7 unable to complete final evaluation. Final: 41 PTMLD: 21 PT: 20	(PTMLD group) Physical therapy programme 3X a week for 4 weeks same as control group. Additional MLD (Vodder method) for 30mins X5 days a week for 4 weeks. MLD performed by 2 certified therapists in week 1, participants perform MLD by themselves in week 2, 3 and 4.	Physical therapy 3X a week x 4 weeks: 10 min warm up, 8 shoulder ROM stretching and strengthening exercises at 6-8 OMNI resistance intensity with supervision of physical therapist. MT for 30 min by skilled therapist (STM + scapular mobilisations), Passive ROM and cool down (10 mins).	Arm volume- circumference in cm Dynamometer AROM – digital inclinometer EORTC QLQ-C30, EORTC QLQ-BR23, DASH, NRS
Dater and Jagtap, 2019 (49) **India**	RCT	20 females: 3 dropped out due to recurrence 7 unable to complete follow up Final: 10 Group A: 5 Group B: 5	Hot moist pack given 10 mins prior to treatment. Given MFR for 90-120 secs on alternate days per week for 1 month	Hot moist pack given 10 mins prior to treatment. Gentle arm flexion and horizontal abduction with wall support stretches 3-5 mins on alternate days for 1 month.	VAS, DASH, shoulder goniometry
Shoukry et al., 2021 (53) **Egypt**	RCT	40 females No dropouts or losses to follow-up Group A: 20 Group B: 20	Low-level laser therapy for 1 month plus PT 3 times a week x 4 weeks. Laser therapy at 1-10,000 Hz, pulse duration from 50 msec to 200 msec. 24~25 min session. PT consisting of AROM exercises, stretching and STM.	3 sessions a week x4 weeks. PT consisting of AROM exercises, passive stretching and STM for 20 mins.	Shoulder Goniometer VAS
Torres-Lacomba et al., 2022 (23) **Spain**	RCT	96 women 1 withdrawal due to lymphoedema Final: 95 AWSPt-G: 48 Control: 47	45 min session 3X a week for 3 weeks. MLD in axilla and proximal ipsilateral arm using resorption strokes (performed on taut cords and distally down the arm) for 20-30 min, followed by progressive AA and active arm exercises: Arm and shoulder stretching exercises, following median nerve neurodynamic glide method for 15-20mins. Home exercises 1-3x a day, 1-3 sets, 5-10 reps.	30min session 3X a week for 3 weeks. Standard active progressive shoulder exercises, functional activities and active PNF. Taught exercises in 1st session, performed at home 1-3X a day, 1-3 sets, 5-10 reps afterwards.	Primary: VAS Secondary: Digital inclinometer OSS FACT-B ARM volume – cm A0 = baseline A1 = After intervention A2 = 3-month follow-up A3 = 6-month follow-up
Xin et al., 2017 (22) **China**	RCT	400 women No dropouts or losses to follow-up MLD+PT: 200 PT: 200	Received health education and self-management 24h prior surgery. PT training like in PT group, with combined MLD by breast-specialist nurse 3X a day for 10 mins from day 0 post-op to discharge, consisting of massage to lymph node areas and then proximally from the distal end of the arm	Received health education and self-management advice 24h prior surgery.4 stages of exercise: 1) <7 post-op: PROM 2) post-drain removed: AROM (wall climbs) 3) post- suture removal: increase AROM, massage shoulder and axilla, return to functional activities 4) >3 months post-op: same as stage 3 with aerobic exercises	Primary: Presence of AWS Secondary: Symptoms of AWS
Liu et al., 2023 (51) **China**	RCT	102 females No dropouts or losses to follow-up MLD: 51 Control: 51	MLD performed by physical therapist. Superficial lymph nodes massaged circumferentially, followed by massage of loose connective tissue, axillary lymph nodes and scar tissue above the wound. Followed by lymphatic drainage massage. Finally, VSD connected to common negative pressure device at 450mmHg was applied	Health education on healthy lifestyles, AWS, establishing confidence, medication, exercise, and nutrition. Advised to do progressive functional exercises: hand grasping, wrist and elbow, followed by shoulder function training for 30min, 3-4X a day for each. After 2 weeks post-op: lateral pulling, lifting, pushing, chest expansion, encircling expansion, lifting and extension 30min, 3-4X a day.	NRS Abduction ROM- universal protractor DASH EORTC QLQ BR23

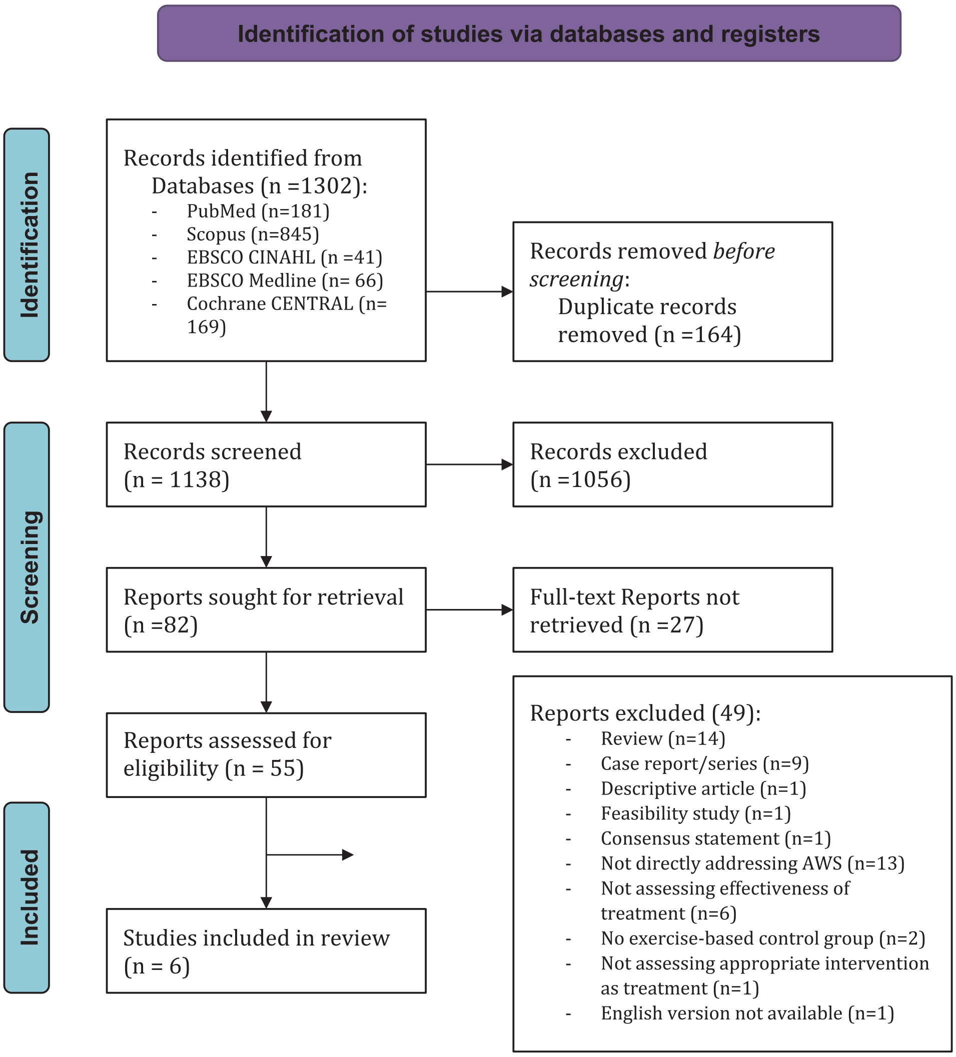

Fig. 1 PRISMA 2020 flow diagram

Results

Selection of Studies

The initial search strategy yielded 1302 studies, of which 164 were removed due to duplication. The title and abstract screening excluded 1056 studies, leaving 82 reports to be sought for retrieval, of which 27 papers did not have the full-text available. Most reports that were not retrieved were registered protocols, which have not yet been published, completed, or lacked links to full texts. Finally, 55 papers were assessed against the eligibility criteria. Forty-nine studies were excluded due to lack of concordance with the eligibility criteria, with twenty-six reports not being the appropriate design. The full reasoning for exclusion is outlined in the PRISMA 2020 flow diagram in Fig. 1. Six studies were included in the review.

Study characteristics

The selected studies for this review consisted of six (75%) RCTs, one (12.5%) quasi-experimental non-randomised trial and one (12.5%) retrospective observational study. All studies were published between 2016 and 2023. Collectively, the six studies recruited 706 participants, of which four dropped out and fourteen were lost before follow-up analysis, resulting in 807 participants being fully examined. The participants ranged from 18–90 years of age. However, Dater and Jagtap[47] did not report any baseline characteristics of their participants. Three studies reported the time gap from the surgery to the onset of intervention, ranging from immediately after patients regained consciousness post-surgery[22], and others beginning 4–6 weeks postoperatively [23, 48]. The main characteristics of each study are outlined in Table 4.

Quality assessment

The results of the quality assessment for the included studies are displayed in Table 5. Each 'yes' was counted as one point and a final score was obtained. The maximum score was 13 based on the tool. A higher score indicated higher methodological quality. Despite all RCTs

Table 5 JBI Critical Appraisal Checklist for Randomised Controlled Trials

Author and Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
Cho et al., 2016 (50)	N	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	10/13
Dater and Jagtap, 2019 (49)	N	N	N	N	N	Y	N	Y	Y	Y	Y	N	Y	6/13
Shoukry et al., 2021 (53)	N	N	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	8/10
Torres-Lacomba et al., 2022 (23)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	12/13
Xin et al., 2017 (22)	N	N	Y	N	N	Y	N	Y	Y	Y	Y	Y	Y	8/13
Liu et al., 2023 (51)	Y	N	Y	N	N	Y	N	Y	Y	Y	Y	Y	Y	9/13

Keys to Q1 – Q13 are presented in Appendix.

identifying as RCTs, only two studies exhibited true randomisation by outlining the randomisation process. This indicates a severe risk of randomisation bias. Only Torres-Lacomba et al.[23)] ensured blinding of participants and allocation concealment to the intervention group, suggesting the presence of performance bias within other RCTs. Likewise, only Cho et al.[48)] reported blinding of the researcher/therapist delivering treatment, indicating a risk of detection bias in other RCTs. The overall quality scores for the RCTs ranged between six and twelve, implying low to moderate risks of bias.

Interventions

Between the selected studies, various rehabilitative options were examined as an effective treatment of AWS. No studies compared the effectiveness of a singular rehabilitative modality to a non-treatment control group, due to ethical issues concerning the withholding of essential post-surgical care. Consequently, in most studies, the intervention groups had the same protocol as the control group, with an additional treatment option. All six studies assessed the effectiveness of PT through mobility exercises, passive, active, active-assisted stretching, proprioceptive neuromuscular facilitation, and progressive functional activities, either as the intervention or as the control intervention. PT focused on increasing the ROM in the shoulder joint through all movements and on maximising mobility in the shoulder girdle, elbow, and wrist. Five studies analysed the use of MLD[22, 23, 48, 49)], of which one study combined MLD with the use of a vacuum seal drainage (VSD)[51)]. The MLD techniques used were Leduc method and Vodder method[50)]. Four studies used MT such as STM, massage, scar or cord mobilisations, and MFR[22, 47, 48, 51)]. One assessed the use of a low-level laser[52)].

All studies implemented their intervention protocols for 3–4 weeks, apart from Liu et al.[49)] and Xin et al.[22)], which did not state the duration of their protocols. However, Xin et al.[22)] emphasised that MLD was performed for 3-days post-surgery and on the day of discharge, followed by PT.

Regarding frequency, interventions ranged from 3–5 times a week with each session lasting between 13–60 minutes. Exercise-based interventions ranged between 3–30 minutes and MLD implementation between 90 seconds- 30 minutes. Two studies included health and postoperative education[22, 49)]. In Dater and Jagtap[47)] both groups received a 10-minute hot moist pack application at the start of their intervention. Details of each intervention are enclosed in Table 4. Only one study[23)] instructed participants to maintain the intervention exercises at home.

Outcomes

Resolution of AWS. The resolution of AWS was examined in two studies[50, 51)], prevention of AWS by a further two studies[22, 23)] and two studies did not investigate the resolution of AWS[47, 51)]. Instead, the two studies focused on the impact of intervention on AWS-associated symptoms, like pain and reduced ROM.

Similar findings were obtained in the control group of Cho et al.[48)], where 65% (n = 13/20) of the group no longer had a visible or palpable cord after 4 weeks of stretching, strengthening, and STM. The intervention group observed greater resolution rates of 71.4% (n = 15/21) when accompanying PT with an additional five sessions of MLD a week, although not significant (p = 0.658). Liu et al.[49)] found health education with functional arm exercises to reduce the tightness caused by cording and facilitated the disappearance of cord-like nodules in the axilla in a mean ±(SD) 26.39 ± 2.31 and 25.87 ± 2.87 days, respectively. Although these findings emphasised the effectiveness of PT in AWS resolution, Liu et al.[49)] found MLD with VSD to produce significantly ($p < 0.001$) shorter durations of clinical appearance of AWS, with tightness and cord-like nodules disappearing in 16.27 ± 2.01 and 16.28 ± 2.13 days.

The studies analysing AWS prevention obtained mixed findings. Xin et al.[22)] discovered that after radical mastectomy, participants selected for MLD with PT, presented with a significantly ($p < 0.05$) lower incidence of AWS at one month (3.5%), two months (2.5%) and three months (1.5%), compared to participants in the PT-only group 10%, 14.5% and 11% respectively. The findings of Torres-Lacomba et al.[23)] showed no adverse effects of the intervention or arm exercises prescribed to the control group for AWS prognosis but did recognise that three (AWSPt = 1, Control = 2) participants had an AWS recurrence due to adjuvant therapies like chemotherapy or radiotherapy.

Quality of life. Only three studies in this review investigated the effect of AWS on HRQoL. Three of the studies used the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ), which is adapted to C30 (general cancer) and BR23 (BC-specific). Cho et al.[48] used both outcome measures and observed significant ($p < 0.01$) mean reductions in breast and arm symptoms in the BR23 scale for both the PTMLD (-20.6 and -20.1 respectively) and PT groups (-17.5 and -23.3 respectively). With C30, the global HRQoL demonstrated increases ($p < 0.01$) of 15.5 in the PTMLD group and 13.0 in the PT group after 4 weeks. Neither outcome measure displayed significant differences ($p < 0.05$) between groups. Liu et al[49] found significant ($p < 0.01$) differences between groups in the HRQoL scores at one month and three months post-intervention, with the MLD and VSD group having greater HRQoL outcomes than the control group by 5.14 (10.8%) at 1-month and 6.11 (13.6%) at 3-months.

Torres-Lacomba et al.[23], used the Functional Assessment of Cancer Therapy – Breast (FACT-B) measure to investigate HRQoL. Their findings were analysed as a total value and between subsections; breast cancer subscale (BCS) and trial outcome index (TOI). FACT-B was not significantly ($p < 0.05$) different between groups at any assessment interval. The BCS and TOI values were significantly larger ($p < 0.01$) in the AWSPt-G compared to the control group at A1 (2.57 and 2.38 respectively) and A2 (3.23 and 3.06 respectively).

Pain. All studies except for Xin et al.[22] investigated the effectiveness of their intervention on post-operative AWS-related pain. Four studies used pain-specific validated outcome measures and one study used a Shoulder Pain and Disability Index (SPADI), which consists of five pain subscales. Cho et al.[48], and Liu et al.[49] all used the Numerical Rating Scale (NRS) to assess changes in pain and obtained significant ($p < 0.05$) reductions in pain post-intervention. Significant decreases were observed by Cho et al.[48] which found a 4-week intervention of MLD and PT to reduce pain by -4.8 ± 1.4, compared to -3.6 ± 1.1 in the PT-only group. The addition of MLD provided a significant ($p < 0.05$) reduction of 1.16 in pain on the NRS, compared to the prescription of stretching, strengthening, and MT mobilisations alone. In terms of longer-lasting outcomes, Liu et al.[49] found mean (±SD) decreases in pain at day one, one month ($p < 0.05$) and three months ($p < 0.05$) post-intervention in both the intervention group 5.72 ± 1.12, 1.23 ± 0.18, 0.76 ± 0.06 respectively, and in the control group 5.73 ± 1.09, 3.12 ± 0.16, 1.23 ± 0.05 respectively. These values equated to an overall 81.5% decrease in pain one-month after intervention in the intervention group, compared to a 48.1% decrease in the control group.

The Visual Analogue Scale (VAS) was also used to assess pain. Combining MFR with a hot moist pack, for 4-weeks, produced a mean -30.0 mm (60%) decrease in VAS scores, in comparison to -10.8 mm (34.6%) in the control group[47]. The differences in VAS scores between-group were significantly lower ($p < 0.05$) in group A than group B. Likewise, Shoukry et al.[51] also obtained significant ($p < 0.05$) reductions in VAS scores, with the low-level laser and PT group obtaining a mean -57.5 mm (84.56%) decrease, and the PT alone group obtaining a -25.0 mm (37.88%) decrease post-treatment. Torres-Lacomba et al.[23] found the greatest differences in VAS scores, with the AWSP-group displaying a mean effect size of -70.94 mm at A_1, and -75.22 mm at A_2, compared to the control group of -49 mm at A_1 and -61 mm at A_2. When comparing the effectiveness of the intervention, there was a significant mean difference ($p < 0.05$) between-groups in favour of MLD with progressive arm exercises at 3 weeks (A_1) -23.94 mm and at 3-month follow-up (A_2) -14.22 mm.

Discussion

To date, AWS continues to be a detrimental post-operative sequela for BC patients, which lacks consensus regarding the optimal management approach[52]. Attempts have been made to encapsulate the most effective treatment for AWS[14, 24], but conclusive research is not yet available. This systematic review aimed to evaluate the effectiveness of adjunct therapies combined with exercise-based interventions compared to exercise-based interventions alone in managing AWS following BC surgery. The findings indicate that combining exercise-focused therapies—such as stretching, mobility exercises, and functional activities—with MT like MLD, low-level laser therapy, or VSD resulted in the best outcomes for AWS resolution, pain reduction, and HRQoL. Similar conclusions were drawn by Agostini et al.[53], who reviewed various treatment options and concluded that MT, specifically STM and MLD with therapeutic exercises, is most beneficial in reducing the course of AWS and enhancing functional recovery. Similarly, Datar & Jagtap[47] found that other conventional therapies such as MFR provided some benefits in reducing pain and improving ROM amongst AWS patients, but it's less effective compared to other therapies. Likewise, De Groef et al.[54] compared the effects of MFR to a standard PT program and found no additional benefit of MFR on pain after BC surgery.

Regarding AWS-related pain, six studies concluded that exercise-based interventions with STM effectively reduce pain on both the VAS and NRS scales. A literature review comparing the reliability, validity, and responsiveness of NRS with VAS found no significant differences in their effectiveness for assessing pain[55]. Anderson[56] explained that NRS and VAS are highly intercorrelated in oncological settings, indicating that scores can be compared to suggest the best intervention. The most significant differences in exercise-only intervention groups were observed by Torres-Lacomba et al.[23] and Cho et al.[48]. However, the validity of pain perception in Cho et al.[48] could have been diminished due to the use of NSAIDs, which were prescribed to all participants. NSAIDs are known for their pain-relieving properties[57], so clinicians should be vigilant when interpreting these findings as NSAIDs can threaten the validity of pain perception. Greater reductions in pain scores were observed when PT was combined with MLD. Studies using NRS found reductions of -4.8 after 4 weeks[48], -4.82 after 1 month[49], and -70.94 mm on the VAS after 3 weeks[23]. These findings can be explained by the increased removal of interstitial fluid and increased lymphatic circulation from MLD[58], which may shift the stagnation of lymph fluid and concentration of inflammatory mediators responsible for hypersensitisation and increased pain perception[31, 59].

Although MLD yielded the most significant pain reduction, other modalities like low-laser therapy also demonstrated significantly greater effect sizes in reducing pain compared to PT alone. This supports the use of multiple modalities when treating patients with AWS, as exercise alone may not be the optimal choice. Nonetheless, all pain findings exceeded the minimal clinically important differences (MCID) for NRS of 1.39 ± 1.05[60] and 9–11 mm for VAS for BC[61], indicating that all studies provided clinically meaningful resolutions for reducing pain associated with AWS. This suggests that physiotherapy is effective in targeting pain, but some interventions produce quicker and more substantial results than others.

HRQoL is increasingly becoming a primary outcome of care within the healthcare system. The included studies showed some disagreement regarding the optimal intervention and its benefits on HRQoL. Cho et al.[48] found that both exercise alone and exercise with MLD had similar effects on HRQoL, with no significant differences between the interventions, suggesting that exercise alone may be sufficient for improving HRQoL. Furthermore, Sánchez et al.[62], who investigated the effects of early intervention on HRQoL for the prevention of secondary lymphoedema and found that early physiotherapy improved HRQoL. Although statistical significance was not achieved, significant differences were found in the physical and social function domains.

In Torres-Lacomba et al.[23], the group performing MLD with progressive exercises had significantly higher BCS and TOI scores, indicating better HRQoL. However, only BCS values at A1 and A2 were clinically meaningful, exceeding the 2-point minimally important difference[65], suggesting MLD with PT may not be as effective for HRQoL improvement as expected. Lovelace et al.[13] highlighted that exercise combined with MLD reduces shoulder dysfunction, scar formation, lymphoedema risk, and joint dysfunction, directly enhancing HRQoL. This implies MLD improves HRQoL subdomains, boosting overall HRQoL. Liu et al.[49] found MLD with VSD led to better HRQoL outcomes than education and functional training, though research on VSD is limited.

This review indicates that exercise can significantly reduce or resolve AWS, with resolution rates of up to 65%[48] after 3–4 weeks. Liu et al.[49] also observed cording disappearing within this timeframe. The most substantial improvement was noted when exercise therapy was combined with STM and MLD, leading to symptom resolution in an average of 16.3 days[49] and a 71% resolution rate[48]. While PT alone is effective, combining it with MLD results in faster and more pronounced effects. Additionally, Fourie and Robb[64] reported spontaneous resolution of AWS within three months. Furthermore, Sandrin et al.[65] suggested using SMM to improve shoulder ROM by breaking fibrotic adhesions but found no better outcomes compared to stretching exercises. Given the unconfirmed aetiology of AWS, careful consideration is needed before using SMM. Literature supports interventions that prevent AWS. Xin et al.[22] found MLD with exercise most effective in preventing AWS, with lower incidence rates in the exercise with MLD group.

A study by Ostos-Díaz et al[66] on early physiotherapy intervention, including education, shoulder ROM exercises, scar and tissue mobilisations, and self-massage, showed significant improvements in postoperative complications. The study reported a 9.3% incidence of AWS at six months but did not specifically investigate physiotherapy's effect on AWS resolution. Scaffidi et al.[67] found early physiotherapy improved functionality and reduced mobility limitations and the need for physiotherapy referrals at 180 days postoperatively. However, some researchers[63, 68, 69] warn that early or vigorous rehabilitation may overstimulate fibrosis production during healing[70, 71], potentially worsening AWS.

In summary, all exercise-based interventions effectively treated AWS and its symptoms, regardless of the variations in the exercises used. The diversity in exercise modes across studies likely reflects the varied clinical practices in exercise prescription and the necessity to tailor exercises to individual patient needs. This variability underscores the diverse clinical presentations of AWS and the absence of standardized grading systems[31]. Ammitzbøll et al.[72] found no additional benefit in managing pain with progressive resistance exercises after ALND compared to usual physiotherapy care, highlighting that exercises need to be specific to the problem, as resistance exercises primarily promote muscle hypertrophy[73] rather than targeting pain.

Strengths and Limitations

While efforts were made to minimize research flaws, this review has some limitations. Some full-text papers could not be retrieved, which might have provided a more comprehensive overview of intervention outcomes. The findings from RCT (randomized controlled trial) studies with lower quality should be interpreted with caution, indicating a higher risk of bias. It is important to note that the variability of evidence-based interventions included in this review may impact its findings. Additionally, some studies implemented certain interventions as a baseline across both groups. For instance, Cho et al.[48] included STM; Dater and Jagtap[47] incorporated a hot moist pack as part of the warm-up prior to exercise; Xin et al.[22] provided health education and self-management advice 24 hours prior to surgery; and Liu et al.[49] offered health education on healthy lifestyles. Thus, the heterogeneity of evidence-based interventions and the inclusion of these interventions as warm-up or cool-down measures may influence the studies' findings, and are potential limitations of this evidence from this review. Nonetheless, this is the first systematic review, including studies from the last 10 years, to investigate adjunct therapies alongside exercise-based interventions for AWS on pain, HRQoL, and resolution.

Clinical Implications and Future Research

This study critically examined various treatment options reported in the literature. The findings recommend management approaches that include shoulder mobility exercises, functional exercises, and stretching, combined with MLD and STM to the axilla and over the cord. These exercises should be tailored to the patient's physical capabilities and needs to enhance outcomes. Clinicians should also consider the timing of implementation, as early physiotherapy showed mixed results for AWS. Other modalities, like VSD, appear effective, but more research is needed to confirm their efficacy. Further research should focus on defining the optimal time to begin physiotherapy and identifying the most effective exercise-based interventions.

Conclusion

Exercise-based therapies are effective in treating AWS and its associated symptoms. However, combining these therapies with MLD is superior, as it treats symptoms more effectively, resolves AWS faster, and prevents its development. Therefore, it is recommended to implement management approaches that include shoulder mobility exercises, functional exercises, and stretching, along with MLD and STM for AWS.

COI:
The authors declare that there are no conflicts of interest

Ethical statrment:
Approval of IRB:N/A

Funding information:
No funding was received

References

1) Cancer Research UK. (2021) What is breast cancer? [Internet]. 2021 [Cited 2023 Mar 20], Available from: https://www.cancerresearchuk.org/about-cancer/breast-cancer/about
2) Lyman GH, Somerfield MR, Bosserman LD, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. Journal of Clinical Oncology. 2017;35(5):561-4.
3) Parker S, Tomlins A. Clinical guidelines for the management of breast cancer. West Midlands Expert Advisory Group for Breats Cancer. 2016.
4) Leidenius M, Leppänen E, Krogerus L, et al. Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer. The American Journal of Surgery. 2003;185(2):127-30.
5) Kell MR, Burke JP, Barry M, et al. Outcome of axillary staging in early breast cancer: a meta-analysis. Breast cancer research and treatment. 2010;120:441-7.
6) Habib AS, Kertai MD, Cooter M, et al. Risk factors for severe acute pain and persistent pain after surgery for breast cancer: a prospective observational study. Regional Anesthesia & Pain Medicine. 2019;44(2):192-9.
7) Wang L, Cohen JC, Devasenapathy N, et al. Prevalence and intensity of persistent post-surgical pain following breast cancer surgery: a systematic review and meta-analysis of observational studies. British journal of anaesthesia. 2020;125(3):346-57.
8) Flowers KM, Beck M, Colebaugh C, et al. Pain, numbness, or both? Distinguishing the longitudinal course and predictors of positive, painful neuropathic features vs numbness after breast cancer surgery. Pain Reports. 2021;6(4):e976.
9) Siddiqui AS, Zeeshan S, Ahmed A, et al. Persistent post-surgical pain following breast cancer surgery: An observational study in a tertiary care hospital. JPMA. The Journal of the Pakistan Medical Association. 2021;71(3):849.
10) Min J, Kim JY, Yeon S, et al. Change in shoulder function in the early recovery phase after breast cancer surgery: a prospective observational study. Journal of Clinical Medicine. 2021;10(15):3416.
11) Van Bemmel AJ, Van De Velde CJ, Schmitz RF, et al. Prevention of seroma formation after axillary dissection in breast cancer: a systematic review. European Journal of Surgical Oncology (EJSO). 2011;37(10):829-35.
12) Bakri NA, Kwasnicki RM, Khan N, et al. Impact of axillary lymph node dissection and sentinel lymph node biopsy on upper limb morbidity in breast cancer patients: a systematic review and meta-analysis. Annals of surgery. 2023;277(4):572-80.
13) Lovelace DL, McDaniel LR, Golden D. Long-term effects of breast cancer surgery, treatment, and survivor care. Journal of midwifery & women's health. 2019;64(6):713-24.
14) Lippi L, de Sire A, Losco L, et al. Axillary web syndrome in breast cancer women: What is the optimal rehabilitation strategy after surgery? A systematic review. Journal of Clinical Medicine. 2022;11(13):3839.
15) Kramer N, Ramjith J, Shamley D. Prevalence of shoulder morbidity after treatment for breast Cancer in South Africa. Supportive Care in Cancer. 2019;27:2591-8.
16) Klein I, Kalichman L, Chen N, et al. A comprehensive approach to risk factors for upper arm morbidities following breast cancer treatment: a prospective study. BMC cancer. 2021;21:1-0.
17) Koehler LA, Blaes AH, Haddad TC, et al. Movement, function, pain, and postoperative edema in axillary web syndrome. Physical therapy. 2015;95(10):1345-53.
18) Moskovitz AH, Anderson BO, Yeung RS, et al. Axillary web syndrome after axillary dissection. The American journal of surgery. 2001;181(5):434-9.
19) Leduc O, Sichere M, Moreau A, et al. Axillary web syndrome: na-

ture and localization. Lymphology. 2009;42(4):176-81.
20) Mullen LA, Harvey SC. Review of axillary web syndrome: What the radiologist should know. European Journal of Radiology. 2019;113:66-73.
21) Dinas K, Kalder M, Zepiridis L, et al. Axillary web syndrome: Incidence, pathogenesis, and management. Current problems in cancer. 2019;43(6):100470.
22) Xin M, Zhang H, Zhong Q, et al. Combining manual lymph drainage with physical exercise after modified radical mastectomy effectively prevents axillary web syndrome. Journal of Phlebology & Lymphology. 2017;10(1).
23) Torres-Lacomba M, Prieto-Gómez V, Arranz-Martín B, et al. Manual lymph drainage with progressive arm exercises for axillary web syndrome after breast cancer surgery: a randomized controlled trial. Physical Therapy. 2022;102(3):pzab314.
24) Koehler LA, Haddad TC, Hunter DW, et al. Axillary web syndrome following breast cancer surgery: symptoms, complications, and management strategies. Breast Cancer: Targets and Therapy. 2018:13-9.
25) Bergmann A, Mendes VV, de Almeida Dias R, et al. Incidence and risk factors for axillary web syndrome after breast cancer surgery. Breast cancer research and treatment. 2012;131:987-92.
26) Torres Lacomba M, Mayoral del Moral O, Coperias Zazo JL, et al. Axillary web syndrome after axillary dissection in breast cancer: a prospective study. Breast cancer research and treatment. 2009;117:625-30.
27) Harris SR. Axillary web syndrome in breast cancer: a prevalent but under-recognized postoperative complication. Breast Care. 2018;13(2):129-32.
28) De Sire A, Invernizzi M, Lippi L, et al. Blurred lines between axillary web syndrome and Mondor's disease after breast cancer surgery: a case report. Annals of physical and rehabilitation medicine. 2020;63(4):365-7.
29) Fukushima KF, Carmo LA, Borinelli AC, et al. Frequency and associated factors of axillary web syndrome in women who had undergone breast cancer surgery: a transversal and retrospective study. Springerplus. 2015;4:1-7.
30) Baggi F, Nevola Teixeira LF, Gandini S, et al. Axillary web syndrome assessment using a self-assessment questionnaire: a prospective cohort study. Supportive Care in Cancer. 2018;26:2801-7.
31) Yeung WM, McPhail SM, Kuys SS. A systematic review of axillary web syndrome (AWS). Journal of cancer survivorship. 2015;9:576-98.
32) Ramírez-Parada K, Garay-Acevedo D, Mella-Abarca W, et al. Axillary web syndrome among Chilean women with breast cancer: incidence and possible predisposing factors. Supportive Care in Cancer. 2020;28:2941-7.
33) Koehler LA, Hunter DW, Blaes AH, et al. Function, shoulder motion, pain, and lymphedema in breast cancer with and without axillary web syndrome: an 18-month follow-up. Physical therapy. 2018;98(6):518-27.
34) Ibrahim RG, Khalaf MM, Elkerm YM, et al. Effect of direct myofascial release and Kinesio Tape on axillary web syndrome. Journal of Medical Sciences, 2018;18(1):1-10.
35) National Institute for Health and Care Excellence (NICE). (2018) Early and locally advanced breast cancer: diagnosis and management. [Internet] 2018 [Cited 2023 Mar 26]. Available from; https://www.nice.org.uk/guidance/ng101
36) Mirandola D, Maestrini F, Carretti G, et al. Effectiveness of an adapted physical activity protocol for upper extremity recovery and quality of life improvement in a ca]se of seroma after breast cancer treatment. International Journal of Environmental Research and Public Health. 2020;17(21):7727.
37) Elan YA, Xiongwei LI, Xiao LO. Diagnosis and treatment of axillary web syndrome: an overview. Chinese Journal of Plastic and Reconstructive Surgery. 2020;2(2):128-36.
38) McNeely ML, Campbell K, Ospina M, et al. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Database of Systematic Reviews. 2010(6).
39) Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021;372.
40) Methley AM, Campbell S, Chew-Graham C, et al. PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC health services research. 2014;14(1):1-0.
41) The Endnote Team. EndNote. 20. [Software] Philadelphia, PA: Clarivate. [Internet] 2013 [Cited 2023 Mar 10]. Available from: https://endnote.com/
42) Gartlehner G, Affengruber L, Titscher V, et al. Single-reviewer abstract screening missed 13 percent of relevant studies: a crowd-based, randomized controlled trial. Journal of clinical epidemiology. 2020;121:20-8.
43) Barker TH, Stone JC, Sears K, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. JBI evidence synthesis. 2023;21(3):494-506.
44) Tufanaru C, Munn Z, Aromataris E, et al. Systematic reviews of effectiveness. Joanna Briggs Institute reviewer's manual. 2017;3.
45) Zeng X, Zhang Y, Kwong JS, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. Journal of evidence-based medicine. 2015;8(1):2-10.
46) Ma LL, Wang YY, Yang ZH, et al. Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: what are they and which is better?. Military Medical Research. 2020;7:1-1.
47) Datar NA, Jagtap V. Effect of myofascial release in axillary web syndrome in carcinoma of breast. Executive Editor. 2019;13(2):105.
48) Cho Y, Do J, Jung S, et al. Effects of a physical therapy program combined with manual lymphatic drainage on shoulder function, quality of life, lymphedema incidence, and pain in breast cancer patients with axillary web syndrome following axillary dissection. Supportive Care in Cancer. 2016;24:2047-57.
49) Liu J, Chen D, Yin X. Effect of manual lymphatic drainage combined with vacuum sealing drainage on axillary web syndrome caused by breast cancer surgery. International Wound Journal. 2023;20(1):183-90.
50) Williams A. Manual lymphatic drainage: exploring the history and evidence base. British journal of community nursing. 2010;15(Sup3):S18-24.
51) Shoukry E, Borhan WH, Selim MM, et al. Effect of low-level laser on axillary web syndrome post mastectomy. The Egyptian Journal of Hospital Medicine. 2021;83(1):1344-9.
52) Da Luz CM, Deitos J, Siqueira TC, et al. Management of axillary web syndrome after breast cancer: evidence-based practice. Revista Brasileira de Ginecologia e Obstetrícia. 2017;39(11):632-9.
53) Agostini F, Attanasi C, Bernetti A, et al. Web axillary pain syndrome—literature evidence and novel rehabilitative suggestions: a narrative review. International Journal of Environmental Research and Public Health. 2021;18(19):10383.
54) De Groef A, Van Kampen M, Vervloesem N, et al. Myofascial techniques have no additional beneficial effects to a standard physical therapy programme for upper limb pain after breast cancer surgery: a randomized controlled trial. Clinical rehabilitation. 2017;31(12):1625-35.
55) Gries K, Berry P, Harrington M, et al. Literature review to assemble the evidence for response scales used in patient-reported outcome measures. Journal of patient-reported outcomes. 2018;2:1-4.
56) Anderson KO. Assessment tools for the evaluation of pain in the oncology patient. Current Pain and Headache Reports. 2007;11:259-64.
57) Ronchetti S, Migliorati G, Delfino DV. Association of inflammatory mediators with pain perception. Biomedicine & pharmacotherapy. 2017;96:1445-52.
58) Ferrandez JC, Laroche JP, Serin D, et al. Lymphoscintigraphic aspects of the effects of manual lymphatic drainage. Journal Des Maladies Vasculaires. 1996;21(5):283-9.
59) Harte SE, Harris RE, Clauw DJ. The neurobiology of central sensitization. Journal of Applied Biobehavioral Research. 2018;23(2):e12137.

60) Kendrick DB, Strout TD. The minimum clinically significant difference in patient-assigned numeric scores for pain. The American journal of emergency medicine. 2005;23(7):828-32.
61) Harrington S, Gilchrist L, Sander A. Breast cancer EDGE task force outcomes: clinical measures of pain. Rehabilitation oncology. 2014;32(1):13-21.
62) Sánchez MJ, Lacomba MT, Sánchez BS, et al. Health related quality of life improvement in breast cancer patients: secondary outcome from a simple blinded, randomised clinical trial. The Breast. 2015;24(1):75-81.
63) Eton DT, Cella D, Yost KJ, et al. A combination of distribution-and anchor-based approaches determined minimally important differences (MIDs) for four endpoints in a breast cancer scale. Journal of clinical epidemiology. 2004;57(9):898-910.
64) Fourie WJ, Robb KA. Physiotherapy management of axillary web syndrome following breast cancer treatment: discussing the use of soft tissue techniques. Physiotherapy. 2009;95(4):314-20.
65) Sandrin F, Nevola Teixeira LF, Garavaglia M, et al. The efficacy in shoulder range of motion of a snapping manual maneuver added to a standardized exercise protocol in axillary web syndrome: a randomized controlled trial. Acta Oncologica. 2023;62(8):969-76.
66) Ostos-Díaz B, Casuso-Holgado MJ, Muñoz-Fernández MJ, et al. Early physical rehabilitation after sentinel lymph node biopsy in breast cancer: is it feasible and safe?. International Journal of Environmental Research and Public Health. 2020;17(22):8382.
67) Scaffidi M, Vulpiani MC, Vetrano M, et al. Early rehabilitation reduces the onset of complications in the upper limb following breast cancer surgery. European journal of physical and rehabilitation medicine. 2012;48:48.
68) Beurskens CH, van Uden CJ, Strobbe LJ, et al. The efficacy of physiotherapy upon shoulder function following axillary dissection in breast cancer, a randomized controlled study. BMC cancer. 2007;7:1-6.
69) Klein I, Kalichman L, Chen N, et al. Effect of physical activity levels on oncological breast surgery recovery: a prospective cohort study. Sci Rep. 2021;11:10432.
70) Robson MC. Proliferative scarring. Surgical Clinics. 2003;83(3):557-69.
71) Wynn TA, Vannella KM. Macrophages in tissue repair, regeneration, and fibrosis. Immunity. 2016;44(3):450-62.
72) Ammitzbøll G, Kristina Kjær T, Johansen C, et al. Effect of progressive resistance training on health-related quality of life in the first year after breast cancer surgery–results from a randomized controlled trial. Acta oncológica. 2019;58(5):665-72.
73) Schoenfeld BJ, Contreras B, Krieger J, et al. Resistance training volume enhances muscle hypertrophy but not strength in trained men. Medicine and science in sports and exercise. 2019;51(1):94.2