DOI: 10.21608/ASJS.2023.298746

Re-alignment of Clavipectoral Fascia for Axillary Web Syndrome Prevention, an Egyptian Multi-Center RCT

Anwar A. Elshenawy, MD;[1] Tarik Abd El-Azim, MD;[2] Ayman Kamal, MD[2]
[1]Department of General Surgery, Faculty of Medicine, Aswan University, Egypt
[2]Department of General Surgery, Faculty of Medicine, Helwan University, Egypt

Introduction: The CPF (clavipectoral fascia) is reported to offer several benefits. It may aid in the reduction of postoperative bleeding and seroma development due to its role in lymph drainage.

Aim of the study: Reporting our experience in re-aligning the CPF after breast surgery with ALND can help avoid the development of AWS.

Patients and methods: A randomized clinical trial for 290 patients undergoing unilateral breast surgery with ALND.

Results: Post-operatively, there was a high significant incidence increase in excised CPF group, regarding seroma formation. Otherwise, there was no difference regarding time for drain removal besides three days drain output.

Conclusion: Pectoral fascia re-alignment has many benefits such as lower incidence of seroma formation, and AWS prevention.

Key words: Pectoral fascia re-alignment, seroma, Axillary web syndrome.

Introduction

Axillary lymph-node dissection (ALND) is crucial in the treatment of breast cancer, as it aids in correct prognosis, recurrence prevention, and the planning of appropriate adjuvant therapy.[1] Complications such as hemorrhage, surgical site infection, axillary web syndrome (AWS), and lymphedema can occur after surgery.[2] AWS is also known by other names such as cording, lymphatic cording, fibrous banding, and, incorrectly, Mondor's illness.[3] AWS is a common complication following ALND breast cancer surgery, with reported rates ranging from 6% to 86 %.[4] The first signs and symptoms appear 2–8 weeks following surgery. In some people, it may be associated to lymphedema. A taut subcutaneous chord in the ipsilateral axilla is a common symptom. As the shoulder is abducted, the cord becomes visible and tight. Arm abduction causes pain, as well as function constraints and a limited range of motion (ROM) in the affected limb.[5] Young age, the scope of surgery, the number of afflicted lymph nodes, seroma throughout the healing phase, and body mass index (BMI) are the most common risk factors.[6] Moskovitz et al.[3] coined the term AWS, but it was first described in 1996 by Ferrandez and Serin as superficial lymphatic thrombosis.[7] The pathophysiology of AWS is mostly shrouded in mystery. Although the lymphatic idea is more widely accepted, venous origin or a combination of both cannot be ruled out.[8] The clavipectoral fascia (CPF) is said to have a number of advantages. Because of its involvement in lymph drainage, it may help to reduce postoperative bleeding and seroma formation.[9] Except when the tumor is located too close to the CPF, CPF is preserved in practically all lumpectomies without producing oncological complications.[10] The purpose of this study is to see if re-aligning the CPF after breast surgery with ALND can help avoid the development of AWS.

Methods

A randomized clinical trial for 290 patients undergoing unilateral breast surgery with ALND at Aswan University hospital (Aswan, Egypt), 15th May Model hospital (Cairo, Egypt), and Helwan University hospital (Cairo, Egypt) from March 2016 to May 2021.

Inclusion criteria

Female patients with early breast cancer and were prepared for conservative breast surgery.

Exclusion criteria

1. Stages III and IV breast cancer.
2. Inflammatory breast cancer.
3. Tumor presented within 5 mm of the CPF.
4. Presence of HTN, DM, or any vascular disorder.

80 patients were omitted from the research; 7 rejected contributions, 60 had HTN, DM or vascular disorder, and thirteen had a deeply placed tumor. 290 patients were involved in the study and randomized into two groups: group I CPF re-alignment patients (N=145) and group II control patients (N=145). Each patient was examined preoperatively, and post-operatively, on hospital discharge (From Day 2 to 6), 4 weeks, and 3, 6 and 12 months after surgery. Furthermore, each subject was examined and informed by the meat research team if they suffered pain. All participants' demographic information was collected during the preoperative assessment, including age, BMI, breast

cancer information, and comorbidities. The patient underwent conservative breast surgery with level II axillary dissection and a suction drain, which was removed when the drain volume was between 20 and 30 ml/day. Data was collected on the number of lymph nodes dissected, seroma formation, infection and tightness feeling, shoulder abduction limitation, and pain in the same arm during post-operative follow-up. In case of pain presence, the patient was again assessed to conclude the etiology, including diagnosis of AWS. Pain reports by the patients and pain form directed the physical examination, to decide the cause of pain. The extent of AWS was assessed by patient's pain report and by inspection and Palpation of the axilla and the arm. The ROM of shoulder abduction was measured using a digital goniometer (Guymon, Model 01129, Lafayette, USA).[11] The pain severity was measured by visual analog scale (VAS). Pain and limited shoulder ROM were diagnostic criteria for AWS, as were apparent or palpable tension cords of tissue in the axilla in the highest shoulder abduction. Inflammatory signs were absent, ruling out superficial thrombophlebitis. According to estrogen receptors (ER), progesterone receptors (PR), human epidermal growth factor receptor (HER2), and proliferation index, our patient received adjuvant therapy (KI67). The study gained permission from all hospitals' research and ethics departments, as well as signed consent from each patient.

Surgical steps

As illustrated in **(Figure 1)**, all surgeries were performed by certified breast surgeons. Skinny flaps were divided abruptly with a scalpel, scissors, and/or the surgeon's fingers. The fascia was removed with the breast in patients with excised CPF to the point where the fibres of the underlying pectoral major muscle (PMM) could be recognized. All levels of CPF were preserved in CPF re-alignment patients. The "peeling off" process started at the PMM's midline and progressed to the inferolateral boundary. ALND of the axilla was performed to levels I–II.

Statistical analysis

Statistical analysis to evaluate differences among both types of parotidectomy concerning surgical complications was performed with the $\chi 2$ test for categorical variables and independent t-test for numerical variables. A P value of less than .05 was considered the level of statistical significance.

Sample-size calculations

To assess the incidence of AWS after ALND with or without clavipectoral fascia preservation we

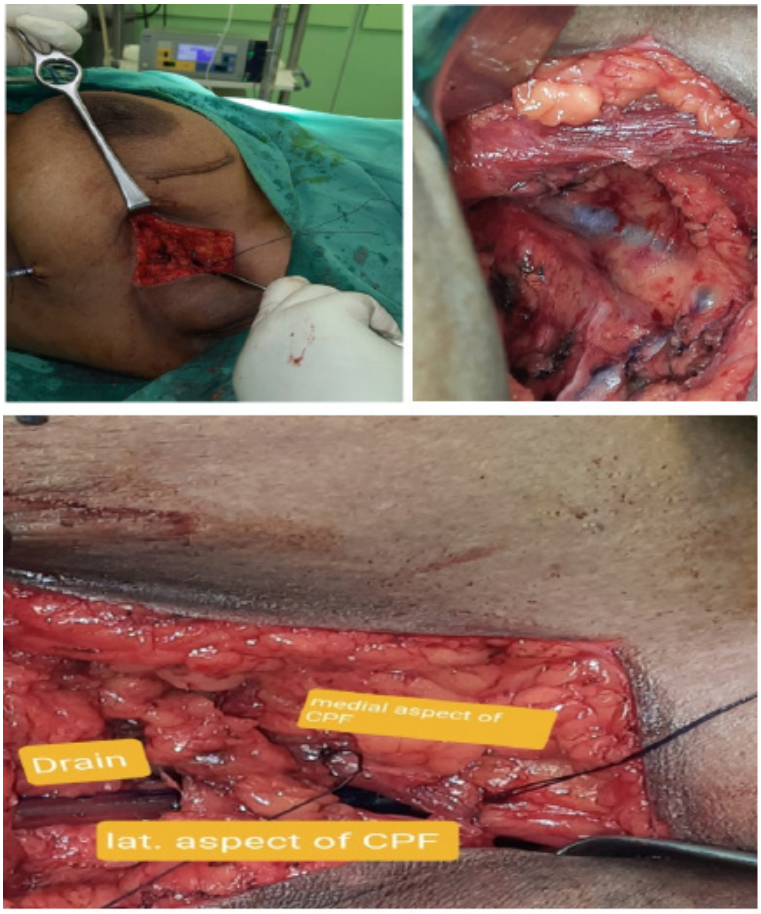

Fig 1: Surgical steps of Mastectomies with ALND with CPF re-alignment.

enrolled 290 women. Sample-size calculation was done supposing an incidence of AWS of 50% in the control group, along with findings in former research (3, 11, 12). With such a sample-size, and after 3% of drop-outs, we can detect an incidence difference of 20% with a precision of 13% at 95% confidence level.

Methods of randomization

Allocation concealment was in place to ensure the individual enrolling of the subject into the study was not a priori knowledge of group assignment. Block randomization occured with randomly mixed block sizes of 2, 4, and 6. The allocator was hiden block size from the executer in order to prevent the executor from predicting the next assignment. Randomization was be carried out by having a piece of paper that has the phrase "Intervention (CPF preservation)" or "Control (No preservation)" placed inside an envelope. The outside of the envelopes was be labeled with the sequence number. After a patient has been enrolled into the study and consented, the next sequence numbered envelope on the stack was opened to determine the study group that the subject entered. For the observational portion of the study, no randomization or blinding occured.

Results

Two hundred and ninety patients with unilateral breast tumor were included; the mean age of the participants was 52.957 ± 6.738 years in CPF re-alignment group and 51.400 ± 5.969 years in the control (CPF excised) group, with no significant difference between two groups (T=1.384, pvalue= 0.169) . The other demographic data of our study are illustrated in **(Table 1).** Regarding intra-operative data, there was no significant difference between two groups in the distance between tumor and CPF (p-value = 0.719), with overall mean distance 27.692 ± 12.378 mm (Range 5:48 mm). The overall mean of the number of excised LN was 15.815 ± 2.780, with no significant difference between both groups. There was no significant difference between the two groups regarding the intra-operative blood loss (p-value = 0.077), and operative time (P-value = 0.759).

Post-operatively, there was a high significant incidence increase in excised CPF group, regarding seroma formation. Otherwise, there was no difference regarding time for drain removal besides three days drain output. The details of postoperative data are shown in **(Table 3).** As illustrated in **(Table 4)**, the incidence of AWS is significant high in excised CPF group (P- value = 0.000). In patients with AWS, the mean VAS was 6.733 ± 7.838 with a significant difference (P-value= 0.000) from the other patients (Mean = 3.278 ± 1.531). Moreover, the ROM was significant lower (Mean = 93.733 ± 19.118) in AWS' patients than other patients (Mean = 128.913 ± 36.873) with p-value 0.000.

Table 1: Demographic data of patients in the study

	Re-aligned CPF group (N=145)	Excised CPF group (N=145)	Tests	P-value
Age (year)	52.957 ± 6.738	51.400 ± 5.969	t= 1.384	0.169
BMI	33.343 ± 0.449	34.433 ± 0.536	t= -1.573	0.118
Tumor stage				
T1	50 (34.48%)	44 (30.34%)		
T2	81 (55.86%)	89 (61.38%)	χ^2= 0.477	0.788
T3	14 (9.66%)	12 (8.28%)		
ER				
Positive	79 (54.48%)	77 (53.1%)	χ2= 0.012	0.914
Negative	66 (45.52%)	68 (46.90%)		
PR				
Positive	81 (55.86%)	75 (51.72%)	χ2= 0.213	0.644
Negative	64 (44.14%)	70 (48.28%)		
HER2				
Positive	77 (53.1%)	73 (50.34%)	χ2= 0.106	0.745
Negative	68 (46.90%)	72 (49.66%)		

ER, estrogen receptor; PR, progesterone receptors; HER2, human epidermal growth factor receptor.

Table 2: Intra-operative data of patients in the study

	Re-aligned CPF group (N=145)	Excised CPF group (N=145)	Tests	P-value
Distance between tumor and CPF (mm)	27.329± 13.492	28.117± 11.036	t= -0.361	0.719
Number of excised LN	15.5± 3.234	16.183± 2.103	t= -1.402	0.163
Intra-operative blood loss	235± 74.867	239.167± 79.773	t= -1.783	0.077
Operative time	80± 17.652	87.083± 27.236	t= -0.307	0.759

CPF, clavi-pectoral fascia; LN, lymph nodes.

Table 3: Post-operative data of patients in the study

	Re-aligned CPF group (N=145)	Excised CPF group (N=145)	Tests	P-value
Seroma formation				
Positive	12 (8.28%)	92 (63.45%)	χ2= 43.271	0.000
Negative	133 (91.72%)	53 (36.55%)		
Time for drain removal	2.357± 0.781	2.383± 0.761	t= -0.193	0.847
Three days drain out-put	240.714± 73.865	240± 74.105	t= 0.055	0.956
Wound infection				
Positive	0	7 (4.83%)	χ2= 3.583	0.058
Negative	145 (100%)	138 (95.17%)		
Fellow up period	31.486± 9.471	30.733± 9.941	t= 0.441	0.660

Table 4: Axillary web syndrome

	Re-aligned CPF group (N=145)	Excised CPF group (N=145)	Tests	P-value
AWS				
Positive	0	36 (24.83%)	χ2= 19.783	0.000
Negative	145 (100%)	109 (75.17%)		
VAS scale	2.671± 1.126	4.850± 2.049	t= -7.653	0.000
ROM	153.886± 19.368	90.983± 19.665	t= 18.330	0.000

AWS, Axillary web syndrome; VAS, visual analogue scale; ROM, range of motion.

Discussion

Over years, AWS had a multiple synonyms; string-like bands, string phlebitis, Superficial lymphatic thrombosis, Mondor disease, cording, webbing, cording lymphoedema, axillary web cord, lymphatic cord, vascular string, syndrome of the axillary cords/adhesion, superficial lymphatic thrombosis, fibrous cords, fibrotic bands, axillary string, aseptic lymphangitis, vascular ring, lymph vessel fibrosis or fiddle string phenomenon.[8] There is a debate regarding the patho-etiology of AWS, but the most accepted theory is lymphatic thrombosis.[13-17] The incidence rate of AWS is supposed to be closely related to the type of axillary LN dissection (ALND or Sentinel lymph node dissection (SLND)), with a range of 0.9% to 25% after SLND, and 5.2 to 36% after ALND.[8] AWS occurs from the first week up to 2 months, postoperatively. [3,6,11,12,14,16,18-27] In our study, the incidence rate was 25% in excised CPF group after ALND.

CPF excision is widely performed in modified radical mastectomy and conservative mastectomy, yet the importance of its excision is still unclear.[28] From embryological point of view, CPF is a part of the muscular anatomy not the glandular tissue of the breast. Furthermore, intraoperatively, the fascia is closely adherent to the pectoralis major muscle (PMM), with no separating epimysium.[29] Consequently, CPF has a vital role with PMM as a myofascial unit particularly in proprioception, as it has multiple nerve endings, decreasing the post-operative bleeding, protects PMM from iatrogenic injury, and prevention of post-operative seroma formation due to its role in lymphatic drainage. In addition, considering the breast cancer as a systematic disease, with no role of any changing local surgical management on overall survival.[30] As a result, excision of CPF is not a proper surgical option.[31]

Dalberg et al.[32] Stated that preservation of CPF

has no risk factor for tumor recurrence provided that tumor not relating to the CPF either clinically or at breast imaging. Deeply seated tumors with excessive nodal spread have the highest incidence of post-operative chest wall recurrence, so that post-operative irradiation is the corner stone in controlling the recurrence.[32] Suijker et al.,[28] in a systematic review, put the rules in patient selection that we could consider in CPF re-alignment technique including; distance between tumor and CPF no more than 5 mm, tumor stage, tumor biology, and adjuvant therapy. The safety distance between the CPF and the tumor (No more than 5 mm) is very important to obtain a clear margin, besides the post-operative radiotherapy to minimize the recurrence rate. We found that no recurrent tumors in a mean post-operative follow-up 31.139± 9.661 months, due to proper selection of cases.

Figueira et al.[33] mentioned that there was a positive co-relation between hypertension and its medical drugs and AWS occurrence, due to their effect on lymphatic flow. On the other hand, DM could protect from AWS because of inhibition of fibrosis process that is supposed to be the main pathology of cords formation. In view of that, we excluded all patients with DM or hypertension from the study. The overall age average of patients suffering from AWS, in our study, was 53.867±5.630 years, while the mean BMI of the AWS patients was 32.067±2.604 kg/m_2 with no significant difference (p-vale<0.05) from the other patients in either age or BMI. Our average age was lower than one mentioned by Johansson et al,[34] (56±10y) and Bergmann et al,[35] (56±13.08y) studies that suggested a positive co-relation between low age, low BMI and AWS incidence, but we did not find any co-relation between BMI or age and AWS appearance (p-value < 0.05).

In overweight and obese patients, the amount of fatty tissue in the armpit area and arm, might obstruct the appearance of visibility or palpation of AWS' cords,[33] thus we put the hypothesis of "re-alignment of CPF" could increase the space between skin and lymphatics, and prevention of AWS pathology besides bad scar disfigurement formation. In our study, the incidence of AWS in re-aligned CPF group was zero with minimal VAS (2.671±1.126) and wide ROM (153.886±19.368). The incidence of AWS in the control group was 25% most of them had moderate limitation of ROM in abduction (Mean=90.983±19.665); this data is similar to the results that mentioned in the literature. The main cause of ROM restriction is the location of the cords in axilla.[27] The degree of pain severity in AWS' patients ranged from 4 to 8 with a mean of 6.733±2.120 with a high significant difference (p-value = 0.000) with the other patient in the control group (Mean=4.222±1.608). The severe pain was found in 35% of AWS' individuals; according to other studies, pain was found in just 13.5% of the cases.[27]

In RCT done by Dalberg et al.[32] the incidence of seroma was lower, but not significant in the CPF preservation group (31% versus 39.8%). Another RCT by Abdelhamid et al,[9] a significant lower frequency of seroma collection was observed in the CPF preservation group of 5.6% versus 24.3%. In our study, seroma formation was significantly higher (P-value= 0.000) in control group (8.571 versus 63.333). Regarding wound infection, there was no significant difference (P-value = 0.058) between the both groups.

Conclusion

Pectoral fascia re-alignment has many benefits such as lower incidence of seroma formation, and AWS prevention. The incidence of tumor recurrence is low in CPF re-alignment, provided that proper selection of the patient.

References

1. Bergkvist L, de Boniface J, Jönsson P-E, Ingvar C, Liljegren G, Frisell J: Axillary recurrence rate after negative sentinel node biopsy in breast cancer: Three-year follow-up of the Swedish Multicenter Cohort Study. ***Annals of Surgery.*** 2008; 247(1): 150-156.
2. Vitug AF, Newman LA: Complications in breast surgery. ***Surgical Clinics of North America.*** 2007; 87(2): 431-451.
3. Moskovitz AH, Anderson BO, Yeung RS, Byrd DR, Lawton TJ, Moe RE: Axillary web syndrome after axillary dissection. ***The American Journal of Surgery.*** 2001; 181(5): 434-439.
4. Koehler LA, Hunter DW, Blaes AH, Haddad TC: 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): 518-527.
5. Koehler L, Haddad T, Hunter D, Tuttle T: Axillary web syndrome following breast cancer surgery: symptoms, complications, and management strategies. ***Breast Cancer: Targets and Therapy.*** 2019; 11: 13.
6. Koehler LA: Axillary Web syndrome ongoing medical evaluation. ***M Library.*** 2013.
7. Serin D, Ferrandez J: Rééducation et cancer du sein. Masson, Paris; 1996.
8. Yeung W, McPhail SM, Kuys SS: A systematic review of axillary web syndrome (AWS). ***Journal of Cancer Survivorship.*** 2015; 9(4): 576-598.
9. Abdelhamid MI, Alkilany MM, Lotfy M: Pectoral

fascia preservation during modified radical mastectomy: Why and when. ***The Egyptian Journal of Surgery.*** 2017; 36(4): 333.

10. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al: Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. ***New England Journal of Medicine***. 2002; 347(16): 1227-1232.
11. Lacomba MT, Del Moral OM, Zazo JLC, Sánchez MJY, Ferrandez J-C, Goni AZ: Axillary web syndrome after axillary dissection in breast cancer: A prospective study. ***Breast Cancer Research and Treatment.*** 2009; 117(3): 625-630.
12. Leidenius M, Leppänen E, Krogerus L, von Smitten K: Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer. ***The American Journal of Surgery.*** 2003; 185(2): 127-130.
13. Rashtak S, Gamble GL, Gibson LE, Pittelkow MR: From furuncle to axillary web syndrome: Shedding light on histopathology and pathogenesis. ***Dermatology.*** 2012; 224(2): 110-114.
14. Marcus R, Pawade J, Vella E: Painful lymphatic occlusion following axillary lymph node surgery. ***British Journal of Surgery.*** 1990; 77(6): 683.
15. Josenhans E: Physiotherapeutic treatment for axillary cord formation following breast cancer surgery. ***Pt_Zeitschrift Für Physiotherapeuten.*** 2007; 59(9): 868-878.
16. Reedijk M, Boerner S, Ghazarian D, McCready D: A case of axillary web syndrome with subcutaneous nodules following axillary surgery. ***The Breast.*** 2006; 15(3): 410-412.
17. Leduc O, Sichere M, Moreau A, Rigolet J, Tinlot A, Dare S, et al: Axillary web syndrome: Nature and localization. ***Lymphology.*** 2009;42(4):176-181.
18. Tilley A, Thomas-MacLean R, Kwan W: Lymphatic cording or axillary web syndrome after breast cancer surgery. ***Canadian Journal of Surgery.*** 2009; 52(4): E105.
19. Craythorne E, Benton E, Macfarlane S: Axillary web syndrome or cording, a variant of mondor disease, following axillary surgery. ***Archives of Dermatology.*** 2009; 145(10): 1199-1200.
20. Kepics JM: Physical therapy treatment of axillary web syndrome. ***Rehabilitation Oncology.*** 2004; 22(1): 21.
21. Fourie W, Robb K: Physiotherapy management of axillary web syndrome following breast cancer treatment: Discussing the use of soft tissue techniques. ***Physiotherapy.*** 2009; 95(4): 314-320.
22. Lattanzi JB, Zimmerman A, Marshall LM: Case report of axillary web syndrome. ***Rehabilitation Oncology.*** 2012; 30(1): 18-21.
23. Koehler L: Axillary web syndrome and lymphedema, a new perspective. ***Lymph Link.*** 2006; 18(3): 9-10.
24. Gurgel C: Axillary web syndrome: Practical implications. ***The Breast Journal***. 2005; 11(6): 531.
25. Aydogan F, Belli AK, Baghaki S, Karabulut K, Tahan G, Uras C: Axillary web syndrome after sentinel node biopsy. ***Breast Care.*** 2008; 3(4): 277-278.
26. Lauridsen MC, Christiansen P, Hessov I: The effect of physiotherapy on shoulder function in patients surgically treated for breast cancer: A randomized study. ***Acta Oncologica.*** 2005; 44(5): 449-457.
27. Bergmann A, Mendes VV, de Almeida Dias R, e Silva BdA, Ferreira MGdCL, Fabro EAN: Incidence and risk factors for axillary web syndrome after breast cancer surgery. ***Breast Cancer Research and Treatment.*** 2012; 131(3): 987-992.
28. Suijker J, Blok YL, de Vries R, van den Tol MP, Krekel NM: Pectoral fascia preservation in oncological mastectomy to reduce complications and improve reconstructions: A systematic review. ***Plastic and Reconstructive Surgery Global Open.*** 2020; 8(3).
29. Stecco C, Macchi V, Porzionato A, Duparc F, De Caro R: The fascia: The forgotten structure. ***Italian Journal of Anatomy and Embryology***. 2011; 116(3): 127.
30. Fisher B: Sounding board. Breast-cancer management: Alternatives to radical mastectomy. ***The New England Journal of Medicine.*** 1979; 301(6): 326-328.
31. Da Silva AV, Rodriguez FR, Loures CM, Lopes VGS: Mastectomy in the era of implant-based reconstruction: Should we be removing the pectoralis fascia? ***The Breast.*** 2012; 21(6): 779-780.
32. Dalberg K, Krawiec K, Sandelin K: Eleven-year follow-up of a randomized study of pectoral fascia preservation after mastectomy for early breast cancer. ***World Journal of Surgery.*** 2010; 34(11): 2539-2544.
33. Figueira PV, Haddad CA, de Almeida Rizzi SK, Facina G, Nazario AC: Diagnosis of axillary

web syndrome in patients after breast cancer surgery. ***American Journal of Clinical Oncology.*** 2018; 41(10): 992-926.

34. Johansson K, Ingvar C, Albertsson M, Ekdahl C: Arm lymphoedema, shoulder mobility and muscle strength after breast cancer treatment? A prospective 2-year study. ***Advances in Physiotherapy.*** 2001; 3(2): 55-66.

35. Bergmann A, Mattos IE, Mattos I, Mattos I, Mattos IE, Mattos IE, et al: Axillary web syndrome after limph node dissection: ***Results of 1004 Breast Cancer Patients.*** 2007.