Martin Martin Jaime (Orcid ID: 0000-0001-6143-6703)
Cuesta Vargas Antonio (Orcid ID: 0000-0002-8880-4315)

Factors Associated with Upper Limb Function in Breast Cancer Survivors

Running title: Upper Limb Function in Breast Cancer

Cristina Roldán-Jiménez, PhD[a,b,+], Jaime Martín Martín, PhD[b,c,+], Bella Pajares, PhD[d], Nuria Ribelles, PhD[e], Emilio Alba, PhD[e], Antonio I Cuesta-Vargas, PhD[a,b,f,*]

[a] Departamento de Fisioterapia, Facultad de Ciencias de la Salud, Universidad de Málaga, Andalucía Tech.

[b] Instituto de Investigación Biomédica de Málaga (IBIMA), Grupo de Clinimetría (F-14).

[c] University of Málaga, Faculty of Medicine, Department of Human Anatomy, Legal Medicine and History of Science; Area of Legal Medicine.

[d] Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga Spain

[e] Hospital Universitario Virgen de la Victoria, Málaga, Spain

[f] School of Clinical Science, Faculty of Health Science, Queensland University Technology, Australia.

[+] Equal contribution

*Corresponding autor:

Antonio I Cuesta-Vargas, PhD[a,b,f],

Email address: acuesta.var@gmail.com

Institutional address: C/ Arquitecto Francisco Peñalosa, 3, PC: 29071, Malaga, Spain.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/pmrj.12731

Funding source.

This research project was partially funded by Contract Nº PS16060 in IBIMA between Novartis-IBIMA (Translation Research in Cancer B-01 & Clinimetric F-14). This consisted of payment for author C.R.J. as physical therapist in the assessment. There is no other relationship with Novartis as partial funder apart from defraying the expenses of employment, and there are no patents, products in development or marketed products relationship to declare according to the definition of financial competing interest.

Acknowledgements

We would like to offer special thanks to the participants if this project. Assistance provided by Cátedra de Fisioterapia of Universidad de Malaga was greatly appreciated

Disclosures

Dr. Alba reports grants and advisory board fees from Roche, advisory board fees from Novartis, grants and advisory board fees from Pfizer, advisory board fees from Lilly, grants and advisory board fees from Bristol-Myers Squibb, advisory board fees from Genomic Health, grants and advisory board fees from Nanostring, non-financial support from Celgene, grants from Sysmex, outside the submitted work.

Factors Associated with Upper Limb Function in Breast Cancer Survivors

Introduction: Breast cancer survivors may suffer side effects from treatment, such as impaired upper limb function after surgery, which may be affected by a range of factors.

Aim: The aim of this study is to analyse the association between upper limb function and strength, fear avoidance, and central sensitisation symptoms among breast cancer survivors, and to explore how these variables are associated with upper limb function.

Design: Validation cohort.

Setting: Institutional Practice at Public Hospital

Patients: 174 breast cancer survivors who had been undergone surgery for a primary tumour.

Interventions: Not applicable.

Main Outcome Measure: Upper limb function was measured by the Upper Limb Functional Index (ULFI-Sp). Independent outcomes were: handgrip strength, which was measured using a Jamar dynamometer on the dominant side; fear avoidance, measured using the Fear-Avoidance Components Scale (FACS-Sp); and central sensitisation symptoms, that were measured using the Central Sensitisation Inventory (CSI-Sp). A linear regression model explaining the ULFI-Sp results was constructed with the variables.

Results: The regression model was significant (F=46.826; p=0.00), and explained 45% of the variance of the ULFI values. All variables showed strong associations with upper limb function.

Conclusions: Greater upper limb function is associated with higher grip strength, lower fear-avoidance behaviour and fewer central sensitisation symptoms among breast cancer survivors. These variables explained 45% of the upper limb function in the regression model, and concur with earlier research showing that factors such as central sensitisation symptoms and kinesiophobia negatively affect upper limb function in such patients. Clinicians should therefore take into account strength, fear avoidance, and central

sensitisation symptoms when considering interventions aimed at improving upper limb function among breast cancer survivors.

Keywords: cancer rehabilitation; disability evaluation; oncology rehabilitation; outcomes assessment/measurement; physical therapy; occupational therapy

Introduction

Breast cancer is a global problem, with approximately two million women diagnosed in 2018[16]. Early diagnosis techniques now provide better prognosis and ensure patient function is less impacted[24,42]. Breast cancer survivors show additional symptoms such as pain, fatigue and psychological stress[2,29], and may also have altered upper limb function or fear of movement (kinesiophobia)[36,37]. There are also risk factors around developing chronic pain in the event of complications from surgery[14].

Treating pain among breast cancer survivors has major therapeutic benefits and can be managed through pharmacological or non-pharmacological interventions[1,34]. Patient education is essential in non-pharmacological interventions[27], while techniques such as self-control of pain, functional and emotional aspects of cancer pain management, and pain relief and its implications all require continuous analysis[29]. Pain can originate from a range of aetiologies, such as neuropathic, nociceptive, or central sensitising pain. Indeed, breast cancer survivors undergoing hormonal treatment have a relatively high risk of suffering from central sensitisation[23]. Central sensitisation is defined as the increased responsiveness of nociceptive neurons due to heightened excitability in the central nervous system in response to stimulus activity, inflammation, and neuronal injury[21].

Kinesiophobia is also present under chronic pain conditions, including among breast cancer survivors[38], where it appears to increase the risk of lymphoedema, depression, and anxiety while at the same time diminishing upper limb function[15]. This circumstance is directly associated with the patient's state of health, meaning kinesiophobia decreases after the rehabilitation process[38]. Pain-related fear avoidance is a common problem among patients suffering from pain, and can lead to them avoiding activities, hypervigilance, and even depression, physical disuse, deconditioning, and disability among the oncology population[5,39,40]. Although fear avoidance among breast cancer

survivors is still unknown, constructs such as kinesiophobia, pain catastrophising, hypervigilance, and avoidance behaviour contribute to disuse, disability, and pain chronification under musculoskeletal conditions[41].

Managing upper limb impairment is fundamental in recovery after cancer treatment, as it can bring both physical and psychosocial benefits[20]. It is therefore vitally important to design systems that allow risk factors that significantly impair upper limb function to be identified[35] and to carry out assessments among breast cancer survivors using a large number of instruments[3]. In this regard, earlier research has studied the way upper limb function contributes to motion, pain and central sensitisation[11]. Upper limb function has also been associated with questionnaires such as the Brief Pain Inventory (BPI)[36]. However, such earlier models did not include FA.

This study aims to analyse the association between upper limb function and strength, fear avoidance, and central sensitisation symptoms among breast cancer survivors, and explore how these variables relate to upper limb function.

Methods

Design

An analytical cross-sectional study was carried out in order to develop an explanatory model of the upper limb's functional limitations with regard to handgrip strength, fear avoidance, and central sensitisation symptoms.

Participants

One hundred and seventy-four breast cancer survivors took part in this study. all of whom had undergone surgery. All participants accepted and signed the informed consent, and the study was approved by the Ethics Committee at the University Clinical Hospital. The Ethics Committee followed the principles set out in the Declaration of Helsinki. All participants were from Virgen de la Victoria University Hospital in Málaga. The inclusion criteria were women aged 18 years or over who had undergone surgery for breast cancer without any recurrence. The exclusion criteria were a lack of reading comprehension and cognitive abilities, as required to fill in the questionnaires.

Measurements

Upper limb function: Upper limb functionality was evaluated in all participants using the Spanish version of the Upper Limb Functional Index (ULFI-Sp). This questionnaire has excellent internal consistency (α=.94) and reliability (r=.93) in healthy adults. The ULFI questionnaire has 25 items graded from 0 to 100, with higher scores indicating greater dysfunction[6]. For statistical analysis, the results of the ULFI-Sp questionnaire were applied in terms of functionality, with higher scores showing greater functionality.

Grip strength was performed using a Jamar dynamometer on both sides[32]. Patients were seated with the shoulder in adduction and neutral rotation, elbow at 90º flexion, and

wrist and forearm in neutral position. The mean of three measurements was used for analysis, with the results shown in kg.

Fear avoidance: The Spanish version of the Fear-Avoidance Components Scale instrument was applied (FACS-Sp). FACS measures three constructs with the FA model: cognitive (pain catastrophising), affective (pain-related fear/anxiety), and behavioural (avoidance) constructs. Furthermore, FACS contemplates the FA-related concept of patient perception of victimisation and blame related to an injury[26]. The FACS-Sp questionnaire has twenty items on a Likert scale from 0 to 5. It is graded from 0 to 100, with higher scores showing greater fear and avoidance behaviours. The instrument has high internal consistency (α=.902), validated in subjects with chronic pain due to musculoskeletal disorders[7] and breast cancer survivors (ω=.91)[17].

Central sensitisation symptoms: The Spanish version of Central Sensitisation (CSI-Sp) was used. CSI shows positive results in internal consistency (α=.872) and test-retest reliability (r=.91)[8], as well as good psychometric properties among breast cancer survivors[33]. It has two sections: section 1 has 25 items broken down into categories (never, rarely, sometimes, often, always), while section 2 deals with medical diagnosis. Higher scores in section A indicate greater symptomatology[8].

Statistical Analysis

Descriptive analyses (mean ± SD) were used for participant descriptive variables (weight, height, BMI, and age), and percentages were applied for discrete variables. T-test for related samples was used to compare grip strength between affected and non-affected sides. A linear regression model explaining the ULFI-Sp results was constructed using all variables with a significant univariate association. Unadjusted and adjusted beta coefficients (B,p) were calculated with one predictor at a time and for each independent

predictor, respectively. The Kolmogorov–Smirnov test showed normal data distribution ($P > .05$). α level was set at 0.05 for all statistical comparisons. SPSS v22.0 was used for all statistical computations.

Results

One hundred and seventy-four breast cancer survivors took part in this study. The age of participants was (50.91 ± 9.23) and body mass index (BMI) was (27.60 ± 5.57). Thirty-seven women (21.2%) were diagnosed with lymphoedema. All women were right-handed, and 59 (34.2%) had undergone surgery on the side of their dominant limb. No significant differences were observed in handgrip strength between affected and non-affected sides (p=0.103). The descriptive results for clinical variables, ULFI-Sp, handgrip, FACS-Sp, CSI-Sp, surgical intervention and cancer-related treatment are shown in Table 1.

Table 1

The regression model was significant (F=46.826; p=0.00). This explained 45% of the variance of ULFI values (R square=0.452, standard error of the estimate=16.519). Unadjusted standardized beta coefficients (calculated with one predictor at a time) and adjusted standardized beta coefficients (calculated for each independent predictor) are shown in Table 2.

Table 2

Discussion

This main findings are that higher levels of upper limb function are associated with greater grip strength, lower fear-avoidance behaviour, and fewer central sensitisation symptoms among breast cancer survivors. These variables explained 45% of the upper limb function in the regression model. As far as the authors are aware, this is the first report on the association of fear avoidance in upper limb function.

The results of this regression model back up earlier research indicating the significant association of factors such as grip strength[11], kinesiophobia[37], and central sensitisation symptoms[12] in upper limb functionality among breast cancer survivors.

Our finding that fear avoidance behavior is negatively associated with upper limb function are in line with the findings of previous studies, which found that kinesiophobia (which is a component of fear avoidance[26]) increases the risk of lympoedema, depression and anxiety, and impaired upper limb function among breast cancer survivors[15].

Moreover, an earlier study found that 40% of the variance related to pain-related disability could be explained directly by kinesiophobia, negative perception of the consequences of the disease, and pain catastrophising among breast cancer survivors[37]. Moreover, patients who are afraid of movement have a lower perceived state of health[38]. Existing literature has shown that signs of central sensitisation, along with pain characteristic, pain catastrophising, range of motion and grip strength, are associated with upper limb function [11]. Specifically, central sensitisation mechanisms alone could explain 40% of the variance in upper limb dysfunction among breast cancer survivors[11]. Other studies have found the presence of central sensitisation symptoms among breast cancer survivors[9], showing a moderate correlation with pain-related disability ($r=0.482$)[37] and a low correlation with pain intensity ($r=0.353$)[12]. Pain severity and higher levels of pain catastrophising also contribute to a higher level of central sensitisation, explaining up to 24% of the variance of CSI[12].

In this study, upper limb function measured by ULFI ranged from 0% to 100%, reflecting the variability of function among breast cancer survivors. These findings are in line with existing literature, which shows that functional limitations can last for a year-and-a-half[25,26] and even up to 6 years following surgery[35].

The mean reported values for the FACS and CSI questionnaires were 30.37 (22.52) and 34.09 (14.74) respectively. Based on established clinical values[25,26], women had mild levels of fear-avoidance and central sensitisation. However, it should be noted that there was heterogeneity in this sample, as seen in the minimum and maximum values (Table 1).

Concerning clinical implications, the results from the present study back up the literature in terms of the influence of grip strength and central sensitisation in upper limb function[11]. Therefore, rehabilitation providers should assess objective measures such as grip strength and patient-reported outcomes such as CSI or FACS to establish central sensitisation and fear-avoidance levels among breast cancer survivors with impaired upper limb function. An objective assessment would allow them to determine which patients would benefit most from a biopsychosocial management approach[13], for example, by integrating pain neuroscience education in patients with predominant central sensitisation pain[10,27,31], or rehabilitation with graded activity[30,38] in those with high levels of fear avoidance. In this regard, while supervised strength exercise can prevent breast cancer-related lymphoedema [4], there is a myth among breast cancer survivors that using the affected arm will exacerbate lymphoedema or increase the risk of developing it[22]. Rehabilitation providers must also consider that the 3 questionnaires used have at least 20 items, although some are already available in short form[28].

Limitations

This study has some limitations. Firstly, several factors associated with upper limb function were not included in the analyses, such as mobility and surgery type[36]. Secondly, psychological factors such as post-traumatic stress[19] contribute to upper limb function

and may also be considered in these patients by the medical team[19]. Future research should further study the association of other factors[18,27,29] with upper limb function.

Conclusion

This study shows that upper limb function is positively associated with handgrip strength and negatively associated with central sensitisation symptoms and fear-avoidance behaviour among breast cancer survivors. These variables explained 45% of the variance of upper limb function values and concurred with earlier research showing that central sensitisation symptoms or kinesiophobia negatively affect upper limb function in these patients. Clinicians should assess these variables using questionnaires such as CSI or FACS in order to ensure better decision-making, always aiming to improve upper limb function among breast cancer survivors.

References

1. van den Beuken-van Everdingen MHJ, de Graeff A, Jongen JLM, et al. Pharmacological Treatment of Pain in Cancer Patients: The Role of Adjuvant Analgesics, a Systematic Review. *Pain Pract Off J World Inst Pain*. 2017;17(3):409-419. doi:10.1111/papr.12459

2. Bjerkeset E, Röhrl K, Schou-Bredal I. Symptom cluster of pain, fatigue, and psychological distress in breast cancer survivors: prevalence and characteristics. *Breast Cancer Res Treat*. 2020;180(1):63-71. doi:10.1007/s10549-020-05522-8

3. Campbell KL, Pusic AL, Zucker DS, et al. A prospective model of care for breast cancer rehabilitation: function. *Cancer*. 2012;118(8 Suppl):2300-2311. doi:10.1002/cncr.27464

4. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. *Med Sci Sports Exerc*. 2019;51(11):2375-2390. doi:10.1249/MSS.0000000000002116

5. Crombez G, Eccleston C, Van Damme S, Vlaeyen JWS, Karoly P. Fear-avoidance model of chronic pain: the next generation. *Clin J Pain*. 2012;28(6):475-483. doi:10.1097/AJP.0b013e3182385392

6. Cuesta-Vargas AI, Gabel PC. Cross-cultural adaptation, reliability and validity of the Spanish version of the upper limb functional index. *Health Qual Life Outcomes*. 2013;11(1). doi:10.1186/1477-7525-11-126

7. Cuesta-Vargas AI, Neblett R, Gatchel RJ, Roldán-Jiménez C. Cross-cultural adaptation and validity of the Spanish fear-avoidance components scale and clinical implications in primary care. *BMC Fam Pract*. 2020;21(1):44. doi:10.1186/s12875-020-01116-x

8. Cuesta-Vargas AI, Roldan-Jimenez C, Neblett R, Gatchel RJ. Cross-cultural adaptation and validity of the Spanish central sensitization inventory. *SpringerPlus*. 2016;5(1). doi:10.1186/s40064-016-3515-4

9. Cuesta-Vargas AI, Roldan- Jimenez C, Pajares B, Alba E. Central sensitization in breast cancer survivors. *J Appl Biobehav Res*. 2018;23(2):e12120. doi:10.1111/jabr.12120

10. De Groef A, Devoogdt N, Van der Gucht E, et al. EduCan trial: study protocol for a randomised controlled trial on the effectiveness of pain neuroscience education after breast cancer surgery on pain, physical, emotional and work-related functioning. *BMJ Open*. 2019;9(1):e025742. doi:10.1136/bmjopen-2018-025742

11. De Groef A, Meeus M, De Vrieze T, et al. Pain characteristics as important contributing factors to upper limb dysfunctions in breast cancer survivors at long term. *Musculoskelet Sci Pract*. 2017;29:52-59. doi:10.1016/j.msksp.2017.03.005

12. De Groef A, Meeus M, De Vrieze T, et al. Unraveling Self-Reported Signs of Central Sensitization in Breast Cancer Survivors with Upper Limb Pain: Prevalence Rate and Contributing Factors. *Pain Physician*. 2018;21(3):E247-E256.

13. De Groef A, Penen F, Dams L, Van der Gucht E, Nijs J, Meeus M. Best-Evidence Rehabilitation for Chronic Pain Part 2: Pain during and after Cancer Treatment. *J Clin Med*. 2019;8(7). doi:10.3390/jcm8070979

14. Divella M, Vetrugno L, Bertozzi S, Seriau L, Carla C, Bove T. Patient-reported pain and other symptoms among breast cancer survivors: prevalence and risk factors. *Tumori*. Published online March 12, 2020:300891620908930. doi:10.1177/0300891620908930

15. Gencay Can A, Can SS, Ekşioğlu E, Çakcı FA. Is kinesiophobia associated with lymphedema, upper extremity function, and psychological morbidity in breast cancer

survivors? *Turk J Phys Med Rehabil*. 2019;65(2):139-146. doi:10.5606/tftrd.2019.2585

16. Global Cancer Observatory. Accessed April 30, 2020. https://gco.iarc.fr/

17. Gutiérrez-Sánchez D, Roldán-Jiménez C, Pajares B, Alba E, Cuesta-Vargas AI. Validity and reliability of the Spanish fear-avoidance components scale in breast cancer survivors. *Eur J Cancer Care (Engl)*. Published online August 23, 2021:e13506. doi:10.1111/ecc.13506

18. Haugen DF, Hjermstad MJ, Hagen N, Caraceni A, Kaasa S, European Palliative Care Research Collaborative (EPCRC). Assessment and classification of cancer breakthrough pain: a systematic literature review. *Pain*. 2010;149(3):476-482. doi:10.1016/j.pain.2010.02.035

19. Kazlauskiene J, Bulotiene G. Prevalence of post-traumatic stress disorder among Lithuanian breast cancer patients and its risk factors. *J Psychosom Res*. 2020;131:109939. doi:10.1016/j.jpsychores.2020.109939

20. Kenyon K, Hebron C, Vuoskoski P, McCrum C. Physiotherapists' experiences of managing upper limb movement impairments due to breast cancer treatment. *Physiother Theory Pract*. 2020;36(1):71-84. doi:10.1080/09593985.2018.1480077

21. Latremoliere A, Woolf CJ. Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity. *J Pain Off J Am Pain Soc*. 2009;10(9):895-926. doi:10.1016/j.jpain.2009.06.012

22. LeVasseur N, Stober C, Ibrahim M, et al. Perceptions of vascular access for intravenous systemic therapy and risk factors for lymphedema in early-stage breast cancer-a patient survey. *Curr Oncol Tor Ont*. 2018;25(4):e305-e310. doi:10.3747/co.25.3911

23. Leysen L, Adriaenssens N, Nijs J, et al. Chronic Pain in Breast Cancer Survivors: Nociceptive, Neuropathic, or Central Sensitization Pain? *Pain Pract Off J World Inst*

Pain. 2019;19(2):183-195. doi:10.1111/papr.12732

24. Liu F-C, Lin H-T, Kuo C-F, See L-C, Chiou M-J, Yu H-P. Epidemiology and survival outcome of breast cancer in a nationwide study. *Oncotarget*. 2017;8(10):16939-16950. doi:10.18632/oncotarget.15207

25. Neblett R, Hartzell MM, Mayer TG, Cohen H, Gatchel RJ. Establishing Clinically Relevant Severity Levels for the Central Sensitization Inventory. *Pain Pract Off J World Inst Pain*. 2017;17(2):166-175. doi:10.1111/papr.12440

26. Neblett R, Mayer TG, Hartzell MM, Williams MJ, Gatchel RJ. The Fear-avoidance Components Scale (FACS): Development and Psychometric Evaluation of a New Measure of Pain-related Fear Avoidance. *Pain Pract Off J World Inst Pain*. 2016;16(4):435-450. doi:10.1111/papr.12333

27. Nijs J, Wijma AJ, Leysen L, et al. Explaining pain following cancer: a practical guide for clinicians. *Braz J Phys Ther*. 2019;23(5):367-377. doi:10.1016/j.bjpt.2018.12.003

28. Nishigami T, Tanaka K, Mibu A, Manfuku M, Yono S, Tanabe A. Development and psychometric properties of short form of central sensitization inventory in participants with musculoskeletal pain: A cross-sectional study. *PloS One*. 2018;13(7):e0200152. doi:10.1371/journal.pone.0200152

29. Odonkor CA, Kim G, Erdek M. Global cancer pain management: a systematic review comparing trials in Africa, Europe and North America. *Pain Manag*. 2017;7(4):299-310. doi:10.2217/pmt-2016-0047

30. Ogston JB, Crowell RD, Konowalchuk BK. Graded group exercise and fear avoidance behavior modification in the treatment of chronic low back pain. *J Back Musculoskelet Rehabil*. 2016;29(4):673-684. doi:10.3233/BMR-160669

31. Pas R, Leysen L, De Goeij W, et al. Pain Neuroscience Education in cancer

survivors with persistent pain: A pilot study. *J Bodyw Mov Ther*. 2020;24(4):239-244. doi:10.1016/j.jbmt.2020.06.027

32. Patterson Merdical. Patterson Medical - strength dynamometer jamar hand. Published 2003. https://www.pattersonmedical.co.uk/app.aspx?cmd=get_item&id=1174

33. Roldán-Jiménez C, Pajares B, Iglesias Campos M, et al. Structural validity and reliability of the Spanish Central Sensitization Inventory in breast cancer survivors. *Pain Pract Off J World Inst Pain*. Published online March 25, 2021. doi:10.1111/papr.13009

34. Santos Salas A, Fuentes Contreras J, Armijo-Olivo S, et al. Non-pharmacological cancer pain interventions in populations with social disparities: a systematic review and meta-analysis. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer*. 2016;24(2):985-1000. doi:10.1007/s00520-015-2998-9

35. Shamley D, Robb K. An early warning surveillance programme for detecting upper limb deterioration after treatment for breast cancer: A novel technology supported system. *BMC Cancer*. 2015;15:635. doi:10.1186/s12885-015-1636-8

36. Smoot B, Paul SM, Aouizerat BE, et al. Predictors of Altered Upper Extremity Function During the First Year After Breast Cancer Treatment. *Am J Phys Med Rehabil*. 2016;95(9):639-655. doi:10.1097/PHM.0000000000000455

37. Van der Gucht E, Dams L, Meeus M, et al. Kinesiophobia contributes to pain-related disability in breast cancer survivors: a cross-sectional study. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer*. Published online January 17, 2020. doi:10.1007/s00520-020-05304-4

38. Velthuis MJ, Peeters PH, Gijsen BC, et al. Role of fear of movement in cancer

survivors participating in a rehabilitation program: a longitudinal cohort study. *Arch Phys Med Rehabil*. 2012;93(2):332-338. doi:10.1016/j.apmr.2011.08.014

39. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain*. 2000;85(3):317-332.

40. Vlaeyen JWS, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. *Pain*. 2012;153(6):1144-1147. doi:10.1016/j.pain.2011.12.009

41. Vlaeyen JWS, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. *Pain*. 2012;153(6):1144-1147. doi:10.1016/j.pain.2011.12.009

42. Yap Y-S, Lu Y-S, Tamura K, et al. Insights Into Breast Cancer in the East vs the West: A Review. *JAMA Oncol*. Published online May 16, 2019. doi:10.1001/jamaoncol.2019.0620

Table 1 Participant descriptive and clinical variables (n=174).

	Mean (SD)	Min-Max
Age (years)	50.9 (9.2)	32.0-70.0
BMI (Kg/m^2)	27.6 (5.5)	17.6-43.5
Years from diagnosis	2.62 (2.2)	0-13.0
ULFI (%)	68.8 (22.1)	0-100
HG dominant side (kg)	21.4 (5.7)	5-35
HG affected side (kg)	20.6 (4.6)	10.3-31.6
HG non affected side (Kg)	21.8 (5.6)	10.3-36.0
FACS-Sp (0-100)	30.3 (22.5)	0-80
CSI-Sp (0-100)	34.0 (14.7)	0-73
Surgical Intervention		Percentage (n)
	Breast-Conserving surgery	66% (115)
	Mastectomy	33.9% (59)
Cancer Treatment		
	Chemotherapy	43.1% (75)
	Radiotherapy	43.1% (75)
	Hormone Therapy	38.5% (67)
	Monoclonal Antibody	12.6% (22)
Current treatment		
	None	24.1% (42)
	Radiotherapy	1.1% (2)
	Monoclonal antibody	6.8% (12)
	Hormone therapy	56.8% (99)

BMI: body mass index; ULFI: *Upper Limbs Functional Index;* HG: *Handgrip*; FACS-Sp: *Fear Avoidance Components Scale (Spanish version);* CSI-Sp: *Central Sensitisation Inventory (Spanish version).*

Table 2. Adjusted and unadjusted standardized beta coefficients from linear regression with upper limb functioning index as the dependent variable.

	Unadjusted Standarized Coefficients		**Adjusted Standarized Coefficients**	
	B	p	B	p
Handgrip	0.258	0,001	0.161	0.006
FACS	-0.508	0,000	-0.243	0.000
CSI	0.606	0,000	-0.461	0.000

FACS-Sp: *Fear Avoidance Components Scale (Spanish version);* CSI: *Central Sensitisation Inventory (Spanish version);* ULFI-Sp: *Upper Limbs Functional Index (Spanish version)*