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Review Article

Postural Alterations in Breast Cancer Patients Undergoing Chemotherapy Treatment

Juana Mª Elía[1]*, Rocío Puerta[1], Aida Ezzedine[1], Martin Núñez[2], Milagros Franco[2], Miriam Lobo[2], Vega Iranzo[3], Victoria Iñigo[1], and Carlos Camps[4]

[1]*Department of Physical Medicine and Rehabilitation, Consorcio Hospital General Universitario de Valencia, Spain*

[2]*Medical Oncology Resident Intern, Consorcio Hospital General Universitario de Valencia, Spain*

[3]*Department of Medicine, Universidad de Valencia, Spain*

[4]*Head of Medical Oncology Service, Consorcio Hospital General Universitario de Valencia, Spain*

***Corresponding author**

Juana Mª Elía, Department of Physical Medicine and Rehabilitation, Consorcio Hospital General Universitario de Valencia, Spain, Email: juanamariaelia@hotmail.com

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Abstract

Breast cancer (BC) is the most common malignant neoplasm in women worldwide. Chemotherapy (CT) remains essential in the treatment of this type of tumour. Patients may present musculoskeletal disorders due to the side effects of CT, which can lead to inability to walk, fall, or fractures associated with balance disorders.

The objective of the present review is to analyse postural alterations in patients with BC undergoing CT. Previous reports both prospective and retrospective cohort studies from 2010 to 2020, were included.

The results show a strong relationship between postural alterations and patients with BC undergoing CT treatment. These data suggest that exposure to CT is an important factor not only for the presence of balance alterations and risk of falls but also for the decrease of quality of life in these patients. These results point out the need to diagnose and assess postural alterations to prevent functional impact in BC patients through exercise programs.

INTRODUCTION

Breast cancer (BC) is the most common malignant neoplasm in women with a higher incidence in developing countries [1,2]. In the last decade survival has increased considerably due to an earlier detection and new treatment options. Nevertheless, despite the improvement in BC cure many patients experience side effects and comorbidities due to antineoplastic treatment [3].

The frequency of disabling neurological complications in cancer patients treated with chemotherapy (CT) has increased considerably in the last years mainly attributable to the intensity of the treatments and the increase in overall survival (OS), which has led to the emergence of late toxic effects. These neurotoxic effects may appear immediately or delayed in time even after long periods since the end of treatment.

Chemotherapy-induced polyneuropathy (CIPN) is the most frequent neurological secondary damage to CT, appearing because of alterations in nerve fibres. It leads to loss of sensation (positional, vibratory, painful and/or thermal) usually in the extremities (characteristically glove and sock distribution). Symptoms can include prickling in fingers and toes (paraesthesia) which becomes painful as it progresses (dysesthesia). CIPN appears after several weeks of treatment, it is usually dose-dependent and show a slow but progressive improvement after stopping CT. Some level of irreversible damage usually persists, though. This damage depends not only on the drug used, but also on the duration of treatment and the accumulated dose of the drug [4-6]. Approximately 30-40% of patients treated with neurotoxic CT show CIPN mainly caused by taxanes [3,4]. Other studies indicate an even higher incidence up to 70% of CIPN during and after treatment, and 40% in cancer survivors [3,7-9].

The clinical course of CINP is highly variable and appears during treatment with the antineoplasic agents or right at the end of the CT treatment. The coasting effect, where the patient worsens weeks or months after stopping the treatment, is infrequent. The onset is usually subacute and progressive if the drug is not reduced or withdrawn.

It is very important that patients could recognise the clinical manifestations that may be warning signs of neuropathy, such as: widening of the base of support when walking, instability or pain when walking (more so in the dark), weakness in the distal part of the limbs, loss of strength in the fingers, difficulty in performing tasks requiring precision, weakness when flexing the ankles,

hearing loss, loss of sensation (also loss of thermal sensation), sensory disturbances (pain perception), disappearance of the osteotendinous reflexes, bowel sounds and disturbance in intestinal motility.

Balance problems and falls are known to occur especially in the first 2 years after CT [3,10]. The risk of falls seems to correlate with increasing CT cycles and doses, as well as higher CIPN scores [11]. When considering the side effects and toxicities of CT it is important to assess balance functions and take precautions in daily life to avoid more serious consequences. Besides, CT is also associated to a loss of bone density related usually to ovarian insufficiency [8,12,13]. It implies a serious problem for patients who already have an increased risk of falling due to impaired postural balance control entailing associated fractures [14].

Assessment of the CINP

Assessment of CIPN is commonly performed through self-reports of functional limitations or neurophysiological tests rather than quantitative assessments of whole-body function. Previous studies have assessed postural balance disturbances using accelerometers, standardized structured tests such as the "Time Up Go" or "Sit To Stand", specific fall risk forms and Fullerton Advanced Balance Scale, among others.

Posturography has proven to be a good diagnostic tool to identify changes in postural balance in elderly patients, diabetic polyneuropathy, or other neurological diseases [15-17]. Currently, early recognition and initial management of CIPN is the only technique to avoid progression to advanced or disabling neuropathy. In fact, there is no effective treatment to prevent the onset of neuropathy. Besides, when it appears there is no way to reverse it, except with the cessation of CT treatment. Sometimes, irreversible damage remains despite even the interruption of CT. Thus, a correct neurological assessment is essential before starting treatment to prevent and treat situations that could aggravate this toxic effect. For some authors, the first step in the symptomatic treatment of CIPN should be an NSAID (combined with of opioids if necessary), being physical rehabilitation and occupational therapy proposed for the most severely affected patients [18]. Knowing how CIPN affects gait and balance can also be the starting point to establish rehabilitation guidelines and restore functional capacity. Overall, these strategies can improve the quality of life of patients undergoing CT.

OBJECTIVES

First, the objective of the present work was to carry out an update on postural alterations in patients with CIPN and BC through a bibliographic review of the recent literature. Second, to review scales and functional assessments most frequently used in clinical practice to identify CIPN and measure the results obtained with the various treatments. Overall, the aim of this work was to achieve the maximum possible evidence for an adequate clinical management of BC patients with CIPN.

MATERIAL AND METHODS

Study design

This is a bibliographic review of the literature to analyse all studies investigating balance disturbances or changes in postural balance and quality of life in BC patients undergoing treatment with CT.

Search strategy

Bibliographic search was carried out of scientific articles published between January 2010 and May 2021 (last date consulted 22/12/2021) on postural changes in BC patients undergoing treatment with CT. References used were both in Spanish and English whose records presented an abstract. The databases consulted were MEDLINE through PubMed, PEDro, Web of Science, Ovid and Cochrane, using the descriptors and search equations shown in the Table 1.

Inclusion and exclusion criteria

Studies of BC patients on CT treatment with at least one balance assessment and preferably CIPN evaluation were considered in this review. Meta-analyses, randomized clinical trials and observational studies were reviewed, although only original manuscripts published in peer-reviewed indexed journals were included. Duplicate articles, those with BC patients not treated with CT, studies with patients older than 65 years, uncompleted or poorly documented studies and were excluded.

Based on the inclusion and exclusion criteria (Tables 2 and 3), the retrieved articles were selected for further review.

Quality assessment of the studies

The PEDro-Spanish scale was used to assess methodological quality. This scale is based on the Delphi list developed by

Table 1: Databases and search equation used.

Databases	Search equation used
PubMed	"Breast cancer" [MeSH Terms] AND "Chemotherapy" [MeSH Terms] AND "Postural balance"
PEDro	"Breast cancer" AND "Chemotherapy" AND "Postural balance"
Web of Science	"Breast cancer" AND "Chemotherapy" AND "Postural balance
Ovid	Breast cancer" AND "Chemotherapy" AND "Postural balance
Cochrane	"Breast cancer" AND "Chemotherapy" AND "Postural balance"

Table 2: Inclusion criteria.

Variables	Inclusion criteria
Design type	Meta-Analyses, randomized clinical trials (RCTs), observational studies
Population	Women with breast cancer; <65 years old undergoing chemotherapy or having received chemotherapy
Published articles	>2010 in English or Spanish

Table 3: Exclusion criteria.

Variables	Exclusion criteria
Inclusion criteria	Failure to meet any of the inclusion criteria
Duplicates	In different data bases/author

Verhagen et al. from Department of Epidemiology in the University of Maastricht (1998). In the mentioned scale, one point is assigned for each affirmative answer and only when the previously established criteria clearly fit. Studies that achieve a score of 9-10 on the PEDro scale are considered to have excellent methodological quality. Similarly, studies with a score between 6-8 have a good methodological quality; between 4-5 a fair quality; and below 4 points are considered to have a poor methodological quality [19] (Annex).

Selection of articles

As mentioned before, duplicated studies were discarded. The relevance of the rest of the references was decided by analysing the titles and abstracts and considering the exclusion criteria. Subsequently, the articles were consulted by reading the full text from the library of the Consorcio Hospital General Universitario de Valencia.

Variables of study

To analyse the same aspects in all the articles and subsequently compare them, a data collection protocol was created. This protocol summarised information about the main publishing characteristics of the study (main author, journal, year, country of publication, language), the objective of the study and characteristics of the sample studied, procedure, results, response to the objective and duration time. An analytical descriptive sheet was designed to accompany each article studied.

RESULTS

Table 4 shows the total number of articles finally retrieved in each of the databases consulted after applying the different search equations, as well as the number of articles selected for bibliographic review according to the selection process followed.

From a total of 65 references retrieved 30, were found to be duplicates and therefore were eliminated. Thus, 35 references were considered valid for the review. Nevertheless, after a slightly first revision, 8 studies were also eliminated because they did not show meaningful data for this review (2 letters to the editor, 3 clinical cases). Afterwards, a deeper review of the full texts led to reject 15 more studies (5 due to sample population over 65 years of age, 1 did not comply with CT treatment and 9 due to methodological flaws). As a consequence, the final number of articles selected for systematic reading was 12 as shown in Figure 1. From the methodological analysis point of view, the type of studies included in the review were observational studies: 8 case-control studies, 3 prospective observational cohort studies and 1 experimental pilot study (Table 5).

The overall quality assessment of the studies included was fair showing an average score of 4.58 (range 4- 5) on the PEDro scale. Fortunately, control groups were like the baseline study. The number of patients in the different studies ranged from 30 to 211. In all cases patients with stage I-III BC were included in the sample. While, two studies included patients with other type of cancer.

In all studies the aim was to assess postural changes in balance caused by CT. The assessment of these changes was performed in almost all of them using static technology tools. Particularly, two studies included dynamic assessment and one study included dynamic assessment exclusively. On the other hand, two studies included assessment of hand grip strength. One of them included assessment of knee extensor strength and the other one included assessment of both forces.

Four studies assessed with reliable and validated scales or tests such as the Fullerton Advanced Balance Scale, Time up go, Sit to Stand and Falls Efficacy Scale (FES).

In relation to the quality of life assessment, three studies used cancer-specific tests like EORTC QLQ-C30 and EORTC QLQ CIPN-20 and CIPNAT. Other generic questionnaires used were International Physical Activity Questionnaire (IPAQ), Brief Pain Inventory (BPI-SF), SF-12 and Multidimensional QOL Scale Patient Version (MQOLSPV).

Follow-up of patients was highly variable in all studies, with the majority being a single assessment, up to 3 months in follow-up cases.

All the studies detected alterations in posture or balance in patients undergoing chemotherapy, even from the first exposure. And in two of them, a progression of these alterations was detected with the accumulation of CT cycles.

Symptoms of CIPN

CIPN symptoms were investigated in 4 studies with validated clinical scales such as the mTNS, NDS and CIPNAT [20-23]. Kneis et al., added electromyography and electroneurography to their evaluation. They detected a significant increase in latency and a decrease in conduction velocity in the lower limbs in the group with cancer. This increase correlated with increase in scores on the clinical scales in these patients. In the other 3 studies, exposure to CT with clinical CIPN showed worse results on functional scales such as EORTC QLQ-C30, EORTC QLQ-CIPN20 or Chemotherapy-Induced Peripheral Neuropathy Assessment Tool (CIPNAT).

Balance control

Nine studies analysed postural changes using technological

Table 4: Number of articles retrieved and selected in each database for deeper review according to selection criteria.

Data bases	Recovered articles	Repeated articles	Selected articles
PUBMED	22	17	5
PEDro	1	1	0
Web of Science	30	0	30
OVID	10	10	0
Cochrane	2	2	0

Authors	Objective	Design	Samples characteristics	Study variables	Results
Kneis et al. (2016)	- To compare balance disturbances in a group of patients with CIPN and a control group.	Case-controls trial (PEDro:4 CT validation scale)	36 patients: -20 BC group completed CT with CIPN -16 control group	Main features: -Displacement of centre of pressures in static posture. -EMG and spinal excitability in bipedal and unipedal posture.	- The swept area displacement of the BC patients was greater than the control group and significantly correlated with self-reported CIPN symptoms (p=0.013). - The BC group revealed prolonged H-wave latency (p=0.021) and increased H-reflex sensitivity from bipedal to monopedal posture (p=0.004).
Bahcaci y Demirbuken (2019)	-To determine whether postural balance was affected by CT cycles.	Observational cohort study (CT Validation Scale PEDro:4)	32 patients with BC (stage I-IIIa)	Main: - Swing intensity by accelerometer during Romberg test; balance tests (unipodal, bipodal and tandem); Sit to Stand and Time Up and Go.	- Less fear of falling between CT cycles (p<0.0125). - No change in bipodal postural posture with eyes open (p=0.734) and eyes closed (p=0.127) - Postural instability in unipodal and tandem posture with eyes open and closed (p=0.000) - Significant increase in STS and TUG instability and test time (p=0.000)
Monfort et al (2016)	- Establish the natural history of postural instability in BC patients undergoing treatment with CT (taxanes).	Pilot study (CT Validation Scale PEDro:4)	32 patients with BC (stage I-III)	Main: - Swept area and velocity measured by static posturometry.	- Increased swept area with eyes closed and progression with cumulative exposure to taxanes (p=0.01). - Persistence of postural instability 1-3 months after termination of lar CT (p=0.002).
Monfort et al. (2017)	- To establish the natural history of CIPN symptoms and functional alterations in BC patients on CT (taxanes) treatment.	Observational cohort study (CT validation scale PEDro:5).	33 patients with BC (stage I-III)	Main: - Swept area and velocity measured by static and dynamic posturometry. Secondary: - EORTC QLQ-CIPN20 - EORTC QLQ-C30 -Brief Pain Inventory (BPI-SF)	- Decreased balance after the first cycle of CT (p=0.016) and progression with cumulative exposure (p=0.001). - Slower gait speed as treatment progressed (p=0.003). - Deficits correlated with increased severity of patient-perceived symptoms on all EORTC QLQ-CIPN20 scales (p<0.05).
Monfort et al. (2019)	- Establish postural impairments in CIPN patients and other cancer survivor populations.	Analytical observational study (CT Validation Scale PEDro:5)	20 patients with BC (stage I-III) or colorectal (stage I-IV): - 6 patients with BC or colorectal after 6 weeks of surgical treatment without having received CT. - 8 patients with BC or colorectal after 6 weeks after CT with mild CIPN symptoms - 6 patients with BC or colorectal after 6 weeks of CT with moderate/severe symptoms of CIPN	Main: - static posturometry with somatosensory, visual and vestibular interference.	The presence of CIPN sensory symptoms was associated with impaired postural control, particularly during eyes-closed balance conditions (p < 0.05).
Evans et al. (2019)	-To compare performance on various static and dynamic balance assessments, with and without a concurrent cognitive task, in women with and without a history of BC. with and without a concurrent cognitive task, in women with and without a history of BC.	Case-controls trial (PEDro:5 CT validation scale)	43 patients -20 patients (Stage I-III) BC -23 controls	Main features: - Static balancing area in a static posture on one leg - NeuroCom Sensory Organization Test (SOT) - Fullerton Advanced Balance Scale (FES) -Time Up and Go Secondary: - IPAQ (International Physical Activity Questionnaire) - FES (Falls Efficacy Scale-International)	- Similar results in swing area on static one-legged stance and SOT between both groups (p>0.005). - Worse results in TUG and FABS in patients with BC (p<0.002)
Moroshita et al. (2018)	- To identify possible loss of balance function and assess the relationship between balance function and muscle strength in healthy and BC patients.	Pilot case-control study (CT validation scale PEDro:5)	33 patients -19 BC patients -14 control cases	Main features: - Body sway test - Hand grip strength - Knee extensor strength -Time Up and Go	-No difference between grip strength or knee extension in the two groups. -Longer TUG time in BC than in healthy subjects (p<0.05). -No postural sway parameters could be related to muscle strength or TUG.
Niederer et al. (2014)	- Cancer patients show lower functional performance compared to the older group, and higher functional performance compared to the older group.	Cross-sectional case-control study (CT valida-tion scale PEDro:4)	65 patients -21 patients with cancer -22 patients aged >65 years -22 control patients	Main -Strength of the knee extensor apparatus - Swept area and velocity measured by static posturometry -EORTC QLQ-C30 -FES (Falls Efficacy Scale-International)	-Gait speed and MIVF of cancer patients were higher than in the older CG (p<0.05). -Fall risk and postural sway were comparable in both groups (p<0.05). -Knee extension strength was lower in the cancer group compared to the age-matched control group (p>0.005).
Winter-Stone et al. (2011)	-To identify neuromuscular, balance and vision factors that contribute to falls in recently treated BC survivors and to explore the links between risk factors for falls and cancer treatment.	Observational study (CT validation scale PEDro:4)	59 patients cancer	- Swept area and speed measured by static posturometry. -Walking speed	-Patients with BC and falls in the last year had lower scores on postural assessments with a pattern of vestibular dysfunction (p<0.01) and delayed letter reading on the sensitivity chart in patients treated with CT (p<0.05) but not with adjuvant endocrine therapy.
Kober el al. (2018)	-To assess differences in demographic and clinical characteristics, sensation, balance, upper limb function, perceived stress, symptom burden between survivors who received paclitaxel and developed (n=153) and did not develop (n=58) CIPN.	Observational study (CT validation scale PEDro:5	211 patients -153 patients with BC with CIPN (Cases) -58 patients with BC without CIPN (Control group)	-Demographic characteristics -Chemotherapy-Induced Peripheral Neuropathy Assessment Tool (CIPNAT) -Time up Go -Fullerton Advanced Scale -Hand grip strength with dynamometer -SF-12	-Survivors with CIPN were older (p=0.001), higher BMI (p=0.009) and higher comorbidity (p=0.00). -Mean CPIN symptomatology duration of 4 years and moderate CIPNAT score. -Lower TUG (p<0.001) and FAB (p<0.001) scores in CIPN survivors. -Worse function, more balance problems (p<0.001), higher symptom burden (p=0.042), higher stress and worse quality of life scores, especially in the functional domain (p<0.008).

				-Multidimensional QOL Scale-Patient Version (MQOLSPV)	
Alves et al. (2019)	- To evaluate the possible correlation between the displacement of baropodometer stabilometric variables and the thermal profiles of cancer patients.	Observational study (CT validation scale PeDro:5)	30 patients -15 patients with BC under treatment (Cases) -15 patients with BC completed treatment >6 months (Control group)	- Thermographic recordings of the lower extremities by infrared thermography - Stabilometric parameters using the FootWork Pro baropodometer with open and closed eyes	- With eyes open, the chemo-radiotherapy group had a high correlation between ML displacement and anterior surface temperature of both legs and the posterior region of the right leg (p=0.018). -High correlation between COP and anterior surface temperature of both legs (p=0.028 right; p=0.046 left). -With eyes closed, no correlation was found between thermography and the stabilometric parameters assessed.
Vallabhajosula et al.(2019)	- To assess whether patients with BC have impaired gait and reduced gait variability and strength compared to individuals without a prior diagnosis of cancer. and strength compared to individuals without a previous diagnosis of cancer.	Observational study (CT validation scale PeDro:5)	34 patients -17 patients with BC completed treatment at least 2 months ago -17 healthy patients (control group)	- Gait: Gait speed, stride length, stride width, stance time, swing time, single stance time and double stance time, support time, swing time, single support time and double support time. -Hand grip strength	- Decreased stride length (p=0.019), decreased gait speed (0=0.048) and increased single stance time in the patient group. - Reduced upper body strength in the patient group (p=0.036).

Table 5: Main characteristics of the studies included in the review (n=12) on the effects on chemotherapy on postural balance of chemotherapy in breast cancer patients between 2010-2020.

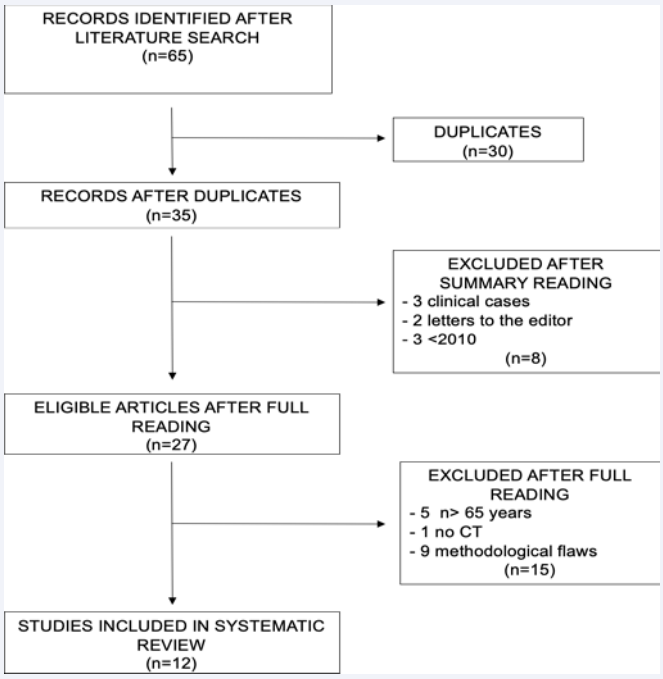

Figure 1 Diagram of the study selection process showing the number of samples included in each research step (n). Initial search PUBMED, PEDro, WOS, OVID and COCHRANE.

tools on static balance control. Niederer et al. [11], and Monfort et al. [21], also added dynamic study, while Vallabhajosula et al. [24], performed dynamic assessment solely. Kober et al. [23], performed subjective postural balance assessment using CIPNAT and they used (Time up go) TUG and FAB (Fullerton Scale) as an objective test.

In 2014, Kneis et al. [20], estimated significant differences in the group of BC patients with CIPN after CT treatment compared to the control group in unipodal support. This correlated with a significant difference in the antagonist co-contraction index, as well as with patient perceived CIPN symptoms. However, there was no difference with bipodal support.

Similar results were reported by Bahaci et al., in 2019 [25], using static and dynamic testing using an accelerometer. The longer the patients were exposed to cycles of CT the bigger were these differences. In contrast, the fear of falling in patients was lower as CT cycles progressed.

In 2016, Monfort et al. [26], reported degradation of all balance assessment parameters in all the patients assessed. There was a clear predominance with eyes closed and the degradation progressed along with the cytostatic exposure.

Later, in 2017 [21], they observed changes in sweep area, step length and gait speed. There was a close relationship between the first and third month of treatment with CT and with

worse self-perceived assessment by the patient. These results were confirmed in 2019, when they reported an increased swept area in patients with CIPN symptoms on posturography with somatosensory, visual, and vestibular interference, being particularly striking in eyes-closed balance conditions.

In 2018, Moroshita et al. [27], presented results with severely impaired TUG in CIPN patients with alterations in the sweep area with open eyes but no reported differences with closed eyes. In agreement with Moroshita's results, Evans et al. [28], assessed an increase in TUG time and decrease in FAB score being these findings compatible with increased risk of falls. Nonetheless, in both study and control groups results were similar when analysing postural changes by registering changes in the sweep area of the centre of pressures. Also, results were similar in both groups under the unipodal support test.

Niederer et al., in 2014[11], included 3 study groups: BC group, healthy age-matched group and healthy>65 years group. Results revealed a greater fear of falling, slower gait speed and lower knee extension force. Moreover, a greater sweep area in the postural assessment of the study group was showed in comparison to the healthy age-matched group. These differences were maintained for the older control group except for gait speed and knee extension strength which was higher in this control group compared to the study population.

In 2011, Winter-Stone et al. [10], concluded that there was a relationship between falls and altered vestibular dysfunction pattern predominantly in the posturographic study in cancer patients with CT treatment completed within the last two years.

Kober et al. [23], performed the only study that did not use technological approach for assessing postural changes. They concluded the strong association between high CIPNAT scores and TUG and FAB with worse outcomes.

The publication by Alves et al., in 2019 [29], described a high correlation between eye open sweep area and leg surface temperature. In contrast, no significant differences were observed in the assessments of postural changes between the study and control groups, probably due to the standardization of the patients' posture during the eyes-closed test.

Vallabhajosula et al. [24], in 2019 performed a dynamic postural assessment presenting all variables (gait speed, step length and single stance time), except swing time variability, were significantly different between all conditions in the study population.

Quality of life and physical function

Different questionnaires and scales to assess quality of life (EORTC-QLQ-C-30, IPAQ, SF-12 and MQOLSPV), fear of falling (FES), pain using the BPI-SF, and level of bothersome symptoms (EORTC- QLQ-CIPN20) were proposed in only 4 of the studies. Significant differences in quality of life and symptomatology were found in longitudinal studies in each CT cycle between groups and among individuals in the same group (Monfort et al. and Niederer et al.) [21]. Evans et al., reported worse TUG and FAB scores that were also correlated with worse FES-I scores in CM patients on QT treatment [28].

Finally, Kober et al., in 2018 described survivors with CIPN showing worse quality of life outcomes especially in the domain of physical functioning as assessed by the SF-12 and MQOLSPV scales [23].

DISCUSSION

This review shows a clear direct association between CT and alterations in parameters of postural balance assessment in patients who receive or have received this oncological treatment.

In the few longitudinal studies found, the alterations are detected from the first cycle of CT and the results worsen in the following cycles where the dose of CT accumulates. These findings are consistent with previous studies in other patient populations [30].

However, some observational studies did not find an increased risk of falls despite an altered assessment of postural balance in these patients as described by Bahaci et al., in 2019 [25].

Furthermore, all parameters were not evaluated in all the studies and there was a large heterogeneity between investigations, such as the time of inclusion in the study from the end of treatment and assessment methods that were not comparable (balance control measured by different techniques, differences in assessment of CIPN across studies and quality of life quantified by different questionnaires).

CIPN symptoms

Four out of twelve studies investigated CIPN symptom levels in BC patients with different methods. The study of Kneis et al., in 2016 showed significant differences in clinical assessment in the control group compared to the study population. It correlated with objective evidence such as increased H-wave latency in the study group and decreased conduction velocity in electoneurophysiological tests [20]. In the results of Monfort, published in 2017 [21], the accumulation of CT cycles raised the mTNS (modified total neuropathy score) in patients especially at the sensory level. It could be of interest in these patients to objectively determine and implement the best measure to assess the signs that appear throughout treatment and their natural history.

Postural balance

Balance monitoring was one of the conditions for inclusion in this review. With one exception, all studies carried out balance assessment using different technological tools with the use of accelerometers and force platforms, with different evaluations and protocols. In addition, 4 studies added assessment using widely validated scales commonly used both in clinical practice and in the literature, such as TUG, Sit to Stand and FAB.

Static balance control was investigated in 10 of the studies and statistically significant alterations were found in all of them. The unipodal balance test was impaired in patients compared to the control group, being more striking when the test was associated with eyes closed, supporting a pattern of vestibular dysfunction. However, in the bipodal support tests there were no differences between the study group and the control group

in some of the [20,25,26]. On the other hand, different reports detected a pattern of visual dysfunction in patients [21,22,28]. In contrast, Moroshita et al., found significant differences in sweep area with eyes open but not with eyes closed [27]. In the same way Alves et al., found differences in thermography and postural changes with eyes open between both study groups, but not with eyes closed [29].

Previous studies in patients with severe peripheral neuropathy secondary to diabetes show similar results in centre-of-pressure velocities of force plate measurements and scores in eyes-closed conditions [30].

Three studies evaluated dynamic balance control [10,21,24], all showing significant alterations in dynamic gait parameters such as gait velocity, step length and bipodal support time.

In a previous review performed by Mustapa et al., in 2016, gait in patients with diabetic neuropathy was described with high double support time, slower speed, and shorter steps as an attempt to maintain gait stability [31]. Similar findings were seen in patients with cancer and CT treatment in this review.

Regarding standardized scales for falls risk assessment in all 4 studies gathered, there were significant alterations that correlated with ratings of technological tools, except for Kober et al. (2018), where no technological assessment was included [23].

Therefore, it appears that CT toxicity affects balance control with predominantly vestibular dysfunction patterns and changes in gait that lead to an increased risk of falls in these patients.

Quality of life and physical function

The quality of life related with health assessed in the studies may be determinant for establishing strategies to improve physical and mental functions. In this regard, the 4 articles that included quality of life assessments reported significant changes in sensory predominance. Also a consequent increase in fear of falling was mentioned as reported by Monfort et al. 2017 [21]. Worse quality of life scores corresponded to patients with more severe balance disturbances. Therefore, the perception of the patient's quality of life is diminished both at a sensitive and functional level, although the latter to a lesser degree.

LIMITATIONS AND CONCLUSIONS

Some limitations must be considered when interpreting the results of this review. First of all, it should be noted that published studies are scarce. The studies analysed had small sample sizes and most of them did not include control groups.

On the other hand, it was not mentioned if surgery could have interfered with the performance of the functional assessments.

Particularities such as if CT treatment was in first, second or third line were not specified either. Also, different treatment times may have influenced the incidence of CIPN.

Other important limitation is the lack of assessment of the optic nerve function that could alter balance, as well as most of the studies only evaluated static alterations. Finally, there was a great heterogeneity in the outcomes measured and the quality of the studies was fair, which did not allow for an unbiased meta-analytic approach.

The results of this review conducted show the existence of a relationship between impaired postural stability and BC patients treated with CT. The results suggest that exposure to CT is an important factor for balance disturbances and increased risk of falls.

The main balance disturbances are static, measured objectively by force platform (9 studies) or accelerometer (1 studies) assessments, obtaining quantitative data from a functional point of view. Dynamic assessment of balance, psychological and/or quality of life assessment, by means of questionnaires or commonly used and approved tools, is scarce.

It is important to identify CIPN symptoms or signs of in order to establish appropriate strategies to avoid more serious or irreversible consequences. Early detection of CIPN can improve the quality of life of BC patients.

More prospective studies are needed to increase statistical significance and improving the quality of this results. This will allow the design of tools for earlier diagnosis of CIPN and the establishment of prevention programmes to improve balance, strength, and quality of life in breast cancer patients undergoing chemotherapy treatment.

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