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MAIN MANUSCRIPT

# Introduction

Cancer is a major public health problem due to its high incidence, morbidity and mortality.<sup>1</sup> According to the latest data published by the International Agency for Research on Cancer, 19 million new cancer cases and nearly 10 million cancer-related deaths were reported worldwide in 2020.<sup>2</sup> Of all types of cancer, those that occur in the breast, lung and colorectum have the highest incidence worldwide.<sup>1,2</sup> These three types of cancer differ in site, stage, level of organic involvement and immunophenotypic characteristics, making them very heterogeneous and variable in diagnosis, treatment and prognosis, and consequently, their course is also markedly different.<sup>3</sup>

Living with cancer is a life-changing experience and the process is full of uncertainties.<sup>4</sup> Cancer patients navigate through different stages known as the *cancer control continuum*, in which the treatment phase is key.<sup>5</sup> During treatment, the patient and their family feel hopeful that it works, but at the same time can feel overwhelmed, afraid of possible adverse effects, while they have to deal with changes to their normal routines.<sup>4</sup>

## Adjuvant chemotherapy and adverse effects

Although there has been great progress in biological and targeted therapies, chemotherapy still plays a major role in the treatment of the aforementioned three cancer sites.<sup>3</sup> According to the current clinical guidelines, due to adjuvant chemotherapy achieving higher rates of cure, increases in survival rates and reductions in the risk of relapse, it is considered the standard treatment for breast cancer<sup>6</sup> and colon cancer<sup>7</sup> in early stages or locally invasive and operable tumors with curative intent. Moreover, many people with breast or colon cancer benefit from chemotherapy thanks to screening programs that allow diagnosis of the disease in early stages. In recent years,

adjuvant chemotherapy has also become a recommended treatment modality for completely resected stage II-III non-small cell lung cancer. So far, however, a low percentage of people with lung cancer benefit from this type of treatment because there is no early screening program for lung cancer and most patients are diagnosed with advanced or metastatic disease, which makes surgery and the subsequent chemotherapy inappropriate.

Though adjuvant chemotherapy has great benefits in terms of achieving disease remission, it is also a highly toxic and aggressive treatment with cumulative adverse effects, often resulting in physical symptoms and even physical decline that are difficult to tolerate. Adverse effects of adjuvant chemotherapy are different for each person depending on their general health, the drugs administered at each cancer site and the schedule and dose used. The most common adverse effects of anthracyclines, taxanes or other combined drugs used in breast cancer are fatigue, infection, hair loss, gastrointestinal disorders, early and late cardiotoxicity, hypersensitivity reactions, peripheral neuropathy, chemo-brain or cognitive dysfunction and nail changes. Similarly, the most common adverse effects of Folfox or Xelox/Capeox used in colon cancer include fatigue and gastrointestinal disorders, but also include peripheral neuropathy, taste disturbance and nail changes. Third Finally, in the case of non-small cell lung cancer, the most frequent adverse effects of carboplatin or cisplatin, taxanes, gemcitabine, pemetrexed and vinorelbine include fatigue, infection, peripheral neuropathy, gastrointestinal disorders, and hypersensitivity reactions, but additionally dyspnea, ototoxicity, nephrotoxicity, and skin toxicity.

#### Adverse effects of chemotherapy and quality of life

Chemotherapy not only affects patients physically but also affects them psychologically and socially, negatively impacting quality of life (QoL) and emotional well-being. Concerning QoL,

some cross-sectional studies have demonstrated that cancer patients on chemotherapy have poorer QoL than the general population, as indicated by lower Physical Component Summary (PCS) scores on the Short form-36 and -12 Health Surveys (SF-36 and SF-12 respectively). 12-16 This means that cancer patients undergoing chemotherapy perceived that they had poorer physical health, with greater limitations in performing moderate or vigorous physical activities and lower performance than they desired. Further, the few longitudinal studies have demonstrated a progressive worsening in physical QoL scores from the start to the middle 17 and the end 18 of chemotherapy treatment.

While there is a consensus on the negative influence of chemotherapy on the PCS as a measure of the physical health component of QoL, there is controversy concerning results with the Mental Component Summary (MCS) as a measure of the mental health component of QoL. Specifically, some studies have found slightly lower MCS scores in cancer patients than the general population, while others detected no differences in the MCS between these populations. Consequently, there is no clear consensus on the impact of chemotherapy on mental health compared to that of the general population. Besides, there is a knowledge gap about QoL regarding differences between patients with cancer at different sites considering the specificities of each site and each type of treatment.

## Emotional well-being in cancer patients during chemotherapy

The National Comprehensive Cancer Network (NCCN) defines distress in cancer as "a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems than can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis". <sup>20(pp5)</sup>

Regarding emotional well-being, most studies have focused on psychological comorbidity in cancer patients in general, reporting rates of 30% to 40%,<sup>21</sup> anxiety and depression being the most prevalent psychological symptoms.<sup>22</sup> A diagnosis of cancer can be psychologically challenging, with a period of adaptation and assimilation during which patients may experience a range of different feelings and emotions, but few cancer patients develop severe mental illness.<sup>23</sup> Despite the importance of knowing the emotional impact of cancer, few studies have examined emotional fluctuation such as changes in positive and negative affect in cancer patients, <sup>24-26</sup> and none have explored these variables in patients receiving outpatient adjuvant chemotherapy.

It is important to highlight that emotional well-being can be measured through affect, which is normally understood as the moods and emotions that are experienced as part of life.<sup>27</sup> Watson and Tellegen<sup>28</sup> divided dimensions of affect into positive and negative, positivity and negativity having to do with pleasant (positive well-being) and unpleasant (emotional distress) moments respectively. Positive affect includes diverse moods and emotions with pleasant subjective content (joy, love, interest in things), that reflect positively on the progress of life, and also refers to the degree to which a person enjoys life and feels enthusiastic, active, strong and energetic. According to Fredrickson, <sup>29</sup> positive emotions activate a type of creative and flexible thinking that facilitates the development of plans and objectives. Further, positive affect increases social resources, specifically through the search for social support, helps develop creativity, strengthens original patterns of action, expands self- and situational awareness, resilience and interpersonality, and is related to a healthy lifestyle. Negative affect includes emotions and states of mind with unpleasant subjective content (anger, sadness, anxiety, worry, guilt, shame, envy, jealousy) and expresses negative reactions of people to their lives, other people or circumstances.<sup>29</sup> Therefore, it may be a sign that life is not going well, and it compromises an individual's well-being.

For health professionals, it is essential to know the emotional well-being of patients to offer care that addresses the emotional needs of patients throughout the cancer trajectory; however, the evidence is incomplete as there is a knowledge gap about the affect of cancer patients in general and those receiving outpatient adjuvant chemotherapy in particular, both overall and by cancer site. Few studies<sup>15</sup> have investigated the impact of cancer longitudinally, capturing possible fluctuations throughout the stages of cancer and during a given stage of cancer (for example, during treatment).

Cancer nurses play a key role in the care of patients receiving outpatient adjuvant chemotherapy. Tollow-up assessment for continuous and personalized cancer management is crucial to meet patients' physical, emotional and practical concerns during cancer treatment, and consequently, contribute to maintaining their perceived QoL and emotional well-being. Nonetheless, current follow-ups are based on a set of assessment criteria that are unlikely to be sufficiently detailed to handle specific features of QoL and affect in cancer patients undergoing outpatient adjuvant chemotherapy and to allow comparisons between different cancer sites. In addition, lack of longitudinal data leads to ignorance of possible fluctuations in QoL and well-being during the treatment phase.

## **Aim**

The aims of this study were to assess whether there are differences in perceived QoL and affect by cancer site in patients with cancer at one of the three sites with the highest incidence (breast, colon and lung) at the start of outpatient adjuvant chemotherapy; to determine whether perceptions change over the course of this type of treatment; and to investigate whether adverse effects have an impact on perceived QoL and affect at the end of the treatment.

#### Methods

## **Study Design and Participants**

This was a multicenter longitudinal descriptive study with two measurement times: start (T1) and end (T2) of the outpatient adjuvant chemotherapy. The sample size estimate for this study was calculated based on the data recorded in the participating hospitals' cancer registries. Based on those data, for this study, for an estimation error of 4.5% and a confidence interval of 95.5% and to achieve adequate statistical power, the estimated sample size required was 218 people (137, 63 and 18 patients with breast, colon and lung cancer, respectively).

Patient recruitment was carried out in four hospital oncology day units (name of the hospitals omitted for blind review). Inclusion criteria were the following: (1) being diagnosed for the first time with breast (C-50), colon-rectosigmoid union (C-18 and C-19, except C-18.1) or bronchial-lung cancer (C-34), without metastasis; (2) starting outpatient systemic adjuvant chemotherapy treatment; (3) being aged between 18 and 70 years; and (4) having given written informed consent, freely agreeing to participate in the study. Exclusion criteria included: (1) previous diagnosis of cancer since it might modulate patients' experiences and perceptions; (2) stage IV (disseminated or metastatic) at the time of diagnosis; (3) poor physical or mental condition; (4) a diagnosis of any severe mental illness; and (5) any language difficulties that made it difficult to complete the self-reported questionnaires.

Of the 410 people selected, 247 met the inclusion criteria and formed the initial sample: 166 people with breast cancer, 62 with colon cancer and 19 with lung cancer, achieving the required sample size.

#### Follow-up and data collection procedure

Data were collected by 10 nurses with extensive experience in cancer patient care and with specific training for this study to ensure uniformity in the data collection process. At the time of the first cycle of treatment, we informed all patients who met the inclusion criteria about the possibility of participating in the study voluntarily and provided information regarding the goals of the study, orally and in writing. At the time of the second cycle, patients were reminded about the study, and those who gave written informed consent were then asked to respond to questionnaires before receiving the second cycle (T1) and again at the end of treatment (T2). The questionnaires were completed in a private room with a nurse researcher collaborating in the study, who was available to clarify their doubts and provide emotional support in event of them having an emotional reaction related to the experience they were going through.

During the data collection process, regular coordination meetings were held between the principal investigator and the nurses to assess potential difficulties, solve problems and uphold the criteria intended to ensure that the process was uniform, as well as to give positive reinforcement and minimize losses to follow-up.

This study was conducted in accordance with the recommendations of the Helsinki declaration and the guidelines of the International Committee of Medical Journal Editors. The protocol was approved by the Clinical Research Ethics Committee of the Basque Country.

#### Measures

**Sociodemographic and clinical variables.** Sociodemographic data were collected through a self-reported questionnaire and clinical data were retrieved from the patient's medical record.

**Quality of life.** QoL was assessed using the SF-12 Health Survey<sup>31</sup>, a shorter version of the SF-36 Health Survey composed of 12 items that measure 8 dimensions and scores can also be summed to yield the Physical Component Summary (PCS) and the Mental Component Summary (MCS).

Like the SF-36, the SF-12 has been found to have excellent psychometric properties in clinical populations, including patients with cancer, and the general population<sup>31</sup> and it has been validated in Spanish.<sup>32</sup> In this study, Cronbach's alpha indicated that the SF-12 had a reliability of  $\alpha_{T1}$ = .72 and  $\alpha_{T2}$ = .72 for the PCS and  $\alpha_{T1}$ = .72 and  $\alpha_{T2}$ = .70 for the MCS.

Affect. Patients' emotional state (affect) was assessed with the Spanish version<sup>33</sup> of the Positive and Negative Affect Scale (PNA)<sup>34</sup>. This scale is composed of 18 items that provide two indicators: positive and negative affect. Positive affect refers to positive emotional states including feeling that things are going your way, that you are pleased because you have got good friends or have accomplished something, and that you are particularly excited or interested in something, full of energy, really enjoying yourself, cheerful, on top of the world, and confident about the future; while negative affect concerns feelings such as being annoyed with someone, and feeling very lonely or remote from other people, very worried, afraid of what might happen, depressed or very unhappy, really tired, restless, wanting to cry and bored. A higher score represents a higher level of the corresponding mood. The internal consistency in this study was good, with Cronbach's alpha values of  $\alpha_{T1}$ = .80 and  $\alpha_{T2}$ = .79 for positive affect and  $\alpha_{T1}$  = .76 and  $\alpha_{T2}$ = .80 for negative affect. Adverse effects. To assess adverse effects, we used an "ad hoc" 15-item questionnaire based on the Common Terminology Criteria for Adverse Events of the National Cancer Institute.<sup>35</sup> We assessed the frequency and severity of each adverse effect with a Likert-type scale where 0 indicated a lack of adverse effects, and 1, 2 and 3 the presence of mild, moderate and severe effects, respectively.

#### **Statistical Analysis**

Analysis of variance for repeated measures was used to compare groups at the start (T1) and the end (T2) of chemotherapy as a function of cancer site, adjusting for sex and age. After the analysis of the variance, post-hoc analysis was performed using the Tukey test to identify significant differences by cancer site. Mean difference effect sizes (Cohen's *d*) were calculated for the corresponding between- and within-group comparisons.

The influence of adverse effects of chemotherapy on QoL and affect was estimated using multiple regression models. Pearson's r was calculated as a crude measure of the association and  $\beta$  coefficients as a measure of the effects of the association adjusted for mean T1 values of the criterion variable, sex, age and cancer site.

#### **Results**

The 247 participants who started the study were between 28 and 70 years of age (M=55.21; SD=9.28) and 188 of them (76.1%) were women. We found statistically significant differences in age (F=31.26; P<.001) between the cancer sites, the mean age of patients with lung cancer (M=62.94; SD=5.37) being higher than that of those with colon cancer (M=59.27; SD=7.81) or breast cancer (M=52.80; SD=9.16). We also found significant differences between cancer sites by sex ( $\chi^2$ =145.8; P<.001): as expected epidemiologically, 98.8% of people with breast cancer were women, compared to 33.9% and 15.8% in the cases of colon and lung cancer, respectively. See Table 1 for data on the other sociodemographic and clinical characteristics. The participants' chemotherapy regimens are detailed in Table 2.

*Insert:* Table 1. Sociodemographic and clinical characteristics of participants overall and by cancer site.

*Insert:* Table 2. Outpatient adjuvant chemotherapy regimens by cancer site.

A total of 234 patients completed the study (T1 and T2), with only 13 losses (5.2%): four patients being withdrawn due to intolerance to treatment and one due to the unexpected development of metastasis, while four withdrew consent and four were lost to follow-up (see Figure).

*Insert:* Figure. Flow of participants through the study.

Table 3 reports the mean scores for the SF-12 and PNA dimensions at the start (T1) and end (T2) of chemotherapy adjusted for sex and age, stratified by cancer site. The multivariate analysis of variance did not indicate any significant differences, though we did observe between-group differences at T1 and within-group effects for the three cancer sites. Specifically, we observed significant differences (*P*<.05) that reflected better Physical and Social Functioning (SF-12), more positive affect and less negative affect in the patients with breast and colon cancer than those with lung cancer. We also found differences at T1 in Role-emotional, Mental Health and MCS scores on the SF-12 between colon and lung cancer groups and in PCS scores between breast and lung cancer groups, this last group obtaining the lowest scores.

In the end-of-treatment comparisons (T2), there were no significant differences between groups; in the cases of Physical Functioning and Mental Health, we observed a possible trend, but differences did not reach significance (P=.088 and P=.091, respectively). Regarding within-group effects, we observed reductions in scores in several QoL dimensions in breast and colon cancer patients, but not in lung cancer patients, in whom scores were more stable. The most notable effects were observed in SF-12 Physical Functioning (d=.59) and PCS (d=.42) scores in the breast cancer

group and in General Health (d=.40) and Social Functioning (d=.51) scores in the colon cancer group. In the case of positive affect, we observed significant decreases in breast (d=.08, P=.015) and colon (d=.32, P=.027) cancer groups, and an increase in the lung cancer group (d=.40, P=.040), while in the case of negative affect, we only observed a significant increase in the colon cancer group (d=.26, P=.007).

Significant differences were found between the groups in both the frequency (F=12.45, P<.001) and severity (F=5.07, P=.007) of adverse effects. Patients in the breast cancer group (M=9.31, SD=3.03) had significantly more adverse effects than those in the colon (M=8.42, SD=2.84, d=.29) and lung (M=7.73, SD=3.13, d=.52) cancer groups. A similar pattern was observed in the severity of adverse effects, although the effect size of the differences was more marked, with the most severe effects in breast cancer (M=1.77, SD=0.27) followed by colon (M=1.59, SD=0.33, d=.65) and lung (M=1.42, SD=0.23, d=1.32) cancer groups.

The impact of the adverse effect severity on QoL was shown to be significant for the SF-12 PCS score (r=-0.13, P=.035), but not its MCS score (r=-0.07, P=.142). The regression model adjusted for sex, age and cancer site and T1 vs T2 PCS scores also showed a significant effect (P=.044), though the effect size should be considered small ( $\beta$ =-.12). We observed a slightly stronger influence of adverse effect severity on affect, with a reduction in positive affect (r=-0.17,  $\beta$ =-.16) and an increase in negative affect (r=0.15,  $\beta$ =.14).

*Insert:* Table 3. Assessment of quality of life and affect at the start (T1) and end (T2) of chemotherapy adjusted for sex and age, stratified by cancer site: Comparisons of differences and effect sizes.

#### **Discussion**

The study provides new knowledge on the perceived QoL and affect at the start of outpatient systemic adjuvant chemotherapy by cancer site comparing the three types with the highest incidence (breast, colon and lung) and contributes to our understanding of changes over the course of this modality of chemotherapy. It also provides insights into the impact of adverse effects on perceived QoL and affect at the end of cancer treatment.

#### Changes in QoL and affect by cancer site

The results of the present study reveal differences in the effects of adjuvant chemotherapy by cancer site. Patients in the breast cancer group, who were younger and had lower levels of comorbidity, showed higher toxicity in terms of both frequency and severity of adverse effects, this being related to notably poorer physical OoL, with greater difficulties in performing activities of daily living and decreases in positive emotions over the course of treatment. While rates of toxicity were not as high as in the breast cancer group, patients with colon cancer also reported a progressive deterioration in their physical QoL during treatment, and though General Health and Social Functioning were the most affected, this was accompanied by worsening of their emotional well-being, with decreasing positive and increasing negative emotions. Patients in the lung cancer group, who were older and had higher levels of comorbidity, started the adjuvant chemotherapy in a very poor state in terms of QoL and emotional affect, but strikingly, both variables remained stable throughout treatment, with even a slight increase in positive emotions. This may be attributable to the chemotherapy agents used for this site being less toxic. However, it might be considered that these patients are so vulnerable at baseline that it is difficult for their state to worsen, as while it remains fairly stable, at the end of the treatment, they continue to report a very poor QoL and marked negative impact on their emotional state.

#### Differences in QoL by cancer site

Regarding QoL, we found a greater impact on the PCS than the MCS in all three groups, a pattern also documented in previous studies with lung<sup>13</sup> and breast cancer patients.<sup>14</sup> We also observed that the three groups analyzed started out from different positions. Notably, the lung cancer group obtained lower scores in the SF-12 PCS and MCS, specifically indicating that these patients started with a more compromised physical health than those with breast cancer and a poorer emotional state than those with colon cancer. Lung cancer, compared to cancer at other sites, is associated with a greater burden of symptoms and a worse prognosis, resulting in higher levels of physical deterioration and psychosocial disorders, with a negative impact on QoL. This may be attributable to the fact that people with lung cancer tend to be more physically and psychologically vulnerable even before they undergo thoracic surgery<sup>36,37</sup> and they also start adjuvant chemotherapy with poorer recovery from surgery,<sup>38,39</sup> which in principle is more aggressive and associated with a greater physical impact than breast or colon cancer surgery. Chen et al.<sup>40</sup> also found that the QoL in patients with resected lung cancer was poor.

Scores in our three groups can be compared with those in other studies that analyzed more heterogeneous samples. For example, in our study, breast and colon cancer patients obtained higher PCS scores and breast and lung cancer patients obtained lower MCS scores than participants in the study of Costa-Requena and Gil<sup>41</sup> in Spain. Considering breast cancer alone, patients in our study obtained lower PCS and MCS scores than those in the studies of Broeckel et al.<sup>12</sup> and Ransom et al.<sup>42</sup> in the USA. Focusing on lung cancer, the PCS score was lower in our study than in that of Etxeberria et al.,<sup>13</sup> though the MCS score was similar.

At the end of the chemotherapy, we did not find significant differences in perceived QoL between the three groups. This is explained by the breast and colon cancer groups obtaining lower scores, closer to those of the lung cancer group. The breast cancer patients reported more physical

worsening, with a notable effect size in the case of the PCS, while colon cancer patients' QoL worsened in both physical and mental domains, as indicated by lower PCS and MCS scores, with a more moderate effect size. In the lung cancer group, we observed a slight worsening in PCS score, with a very small effect size, but at the same time, these patients showed an improvement in MCS score, with a moderate-to-low effect size. That is, while the breast and colon cancer patients felt that their QoL had worsened, perceptions among the lung cancer patients were fairly stable and even slightly improved. Nevertheless, we should underline that the lung cancer patients started in a worse position in terms of their perception of their health, and they still obtained worse scores at the end of the chemotherapy than those in the other groups. In other words, lung cancer patients have the most compromised OoL both before and after treatment.

In summary, the effects of chemotherapy seem to limit patients more physically than mentally. Its cumulative effect tends to worsen over time, especially in patients with breast cancer. The MCS did not show very relevant changes. It should be noted that patients with lung cancer were the group that showed the worst perceived QoL both at the start and the end of the chemotherapy.

#### Differences in affect by cancer site

Regarding affect, our analysis reveals changes in emotional state that were not reflected in changes in the MCS. As with QoL, differences were also found between the three groups in affect.

At the start of chemotherapy, patients with lung cancer reported a less positive emotional state than patients with breast and colon cancer, with feelings that things were not going their way, as well as feeling less excited or interested in things, with less energy, enjoying things less, and being less cheerful, less confident about future and less satisfied with their achievements. The lung cancer patients also showed greater negative affect than the colon cancer group, with more feelings

of being annoyed with someone, loneliness, worry, fear of what might happen, depression or unhappiness, tiredness, restlessness, wanting to cry and boredom. That is, concerning the balance of positive and negative emotions, the lung cancer patients were seen to be in a more vulnerable emotional state at the start of the treatment. Zabora et al.<sup>43</sup> also found the highest intensity of psychological distress in patients with lung cancer among a total of 14 cancer sites. This emotional vulnerability of patients with lung cancer could be explained by self-perceived life expectancy, prognosis and threat of death being worse among these patients than those with cancer at other sites, an issue that should be investigated in greater depth.

At the end of the chemotherapy, we observed different trends in the three groups. There was a reduction in positive affect in the breast and colon cancer patients, while interestingly the lung cancer patients, who were in a highly vulnerable emotional state at the start of the treatment, showed notable improvements in terms of positive emotions. In the case of negative affect, the feelings of worry, fear, tiredness, restlessness, etc., grew among the colon cancer patients, whereas no significant changes were observed in the other two groups. This could be because, as noted in previous studies, poor physical health goes hand in hand with a poor emotional state in patients on chemotherapy. 44,45 In this regard, in the case of colon cancer patients, the adverse effects appear more gradually and at the start of chemotherapy tend to be better tolerated than those in cancer at the other two sites analyzed.

While there was a slight improvement in the lung cancer patients, the emotional state of colon cancer patients substantially worsened. Although at the end of the treatment the differences in positive and negative affect between the three groups weakened, the scores indicate a very vulnerable emotional state across all the groups. This analysis of affect again indicates different trends in the three groups, somewhat similar to the pattern found in the analysis of QoL.

#### Impact of adverse effects on perceived QoL and affect

We assessed whether the development of adverse effects influenced perceived QoL and affect at the end of the chemotherapy, regression analyses indicating that adverse effects contributed slightly to reducing PCS. This is in line with previous research, such as the study of Huang et al.,<sup>46</sup> which indicated that women with breast cancer who perceived symptoms to be more severe obtained lower PCS, and that of Deshields et al.,<sup>47</sup> who found that the more symptoms experienced, the poorer the patients perceived their QoL. Ransom et al.<sup>42</sup> also showed that greater focusing on symptoms was associated with less improvement in PCS.

In regression analyses, we observed that adverse effects are associated with lower positive affect and higher negative affect. This is in line with the observations of Baumeister et al.<sup>48</sup> and Páez et al.,<sup>49</sup> who indicated that negative events diminish positive affect and reinforce negative affect. Research such as that of Pressman and Cohen<sup>50</sup> indicates that positive affect in patients with serious diseases, such as cancer, may be diminished, especially in the early stages of the disease, but it is never absent.

In brief, at the start of chemotherapy, we found different patterns in perceived QoL and affect in patients with breast, colon and lung cancer, and these differences lessened by the end of the treatment due to specific changes occurring in each group. It is also worth noting that, in this study, the assessment of affect using the PNA revealed an emotional impact that was not reflected in SF-12 scores, either in the separate mental health dimensions or the MCS. That is, we identified emotional changes that were not captured by the QoL scale.

# **Strengths and Limitations**

This study has some strengths and limitations. Regarding strengths, to our knowledge, this is the first longitudinal study that has assessed in parallel differences in QoL and positive and negative

affect in patients with breast, colon and lung cancer undergoing outpatient adjuvant chemotherapy and compared the results by cancer site. The focus of this study was to improve our understanding of the experience of cancer patients undergoing outpatient adjuvant chemotherapy treatment. We sought to obtain relatively homogeneous samples, by focusing on only the three cancer sites with the highest incidence worldwide and in which this modality of chemotherapy is widely used for curative purposes. Another strength is that this study has been able to detect emotional changes using the PNA scale, even in patients with potentially curable disease, which may have been underestimated in other studies using other measurement instruments.

One limitation of the study is that, although it was planned as a controlled study, seeking to stratify patients based on incident tumors and obtain a representative sample of patients for each group, the final lung cancer group contained only 19 patients, which reduced the statistical power, weakening the statistical analysis. Nevertheless, while the differences were not statistically significant in some of the comparisons, in many cases we observed a moderate effect size, and this suggests that despite not reaching statistical significance, the analysis does allow us to explore potentially relevant clinical changes. Future research would require larger numbers of lung cancer patients to overcome this statistical weakness. Another limitation is that changes in perceived QoL and emotional state may be explained by numerous factors which have not been considered in this study, such as social support and psychological variables like coping strategies and resilience. This suggests new lines of research that investigate these variables and also include a qualitative perspective, allowing the description of factors that might explain changes observed.

# **Clinical Implications**

These findings have implications for practice, in particular, that as well as assessing QoL of cancer patients with tools such as the SF-12 or -36, we should use other types of instruments, such as the

PNA, that are more sensitive and allow us to detect and visualize changes in emotional well-being, rather than placing emphasis on psychological comorbidity that is not always present. Hence, we recommend the use of more sensitive complementary instruments to properly assess emotional well-being and affect.

The results of this study highlight the need to consider differences by cancer site and establish a multidisciplinary systematic physical and psychological support system from the start of treatment, even from diagnosis. This would help health professionals to identify early emotional impact and enhance the monitoring of the most vulnerable individuals, in this case, the lung cancer group, though without neglecting the needs of the other two groups. This would guide the provision of specific and personalized follow-up and emotional support, and referral of individual patients to other resources as appropriate. In turn, all these clinical implications open new avenues for research, especially considering the differences detected between cancer sites.

Cancer nurses, as part of the multidisciplinary cancer team, play a fundamental role not only in the safe administration of adjuvant chemotherapy treatment but also in the monitoring, accompaniment and assessment of physical and emotional well-being of patients undergoing treatment. By providing personalized health education based on the known adverse effects of each chemotherapy regimen at each cancer site, they can contribute to strengthening patients' self-monitoring including the perception of adverse effects. This would help them anticipate problems, and hence, learn to self-care and manage support medication. This should help patients to feel more in control of their situation and the proper relief of symptoms would help them to continue with their usual activities, improving their perceived health and, consequently, maintaining perceived QoL. It is also important that cancer nurses promote positive affect in these patients through interventions that help develop more positive attitudes and feelings towards themselves

and that help maintain autonomy and a sense of control of the situation. Nursing interventions to lessen negative affect with strategies to reduce the focus of negative thoughts, increase the feeling of ability to cope and promote emotional-informational support should be designed. This way, patients will be able to mitigate negative affect and also maintain or increase positive emotions that help to relieve symptoms of physical discomfort<sup>50</sup> and consequently improve perceived OoL.<sup>24,26</sup>

### **Conclusions**

The findings of this study showed that, regarding QoL, the differences between the three groups of patients were mainly notable at the start of chemotherapy and mainly in physical health (PCS). While differences were less evident in the mental health component (MCS) of the SF-12, the complementary study of affect allowed us to identify relevant differences in emotional state between groups at the start and within groups during treatment. Notably, the lung cancer patients had more compromised health, and hence, may be considered an at-risk group that should have more focused or intense care seeking to improve their health from the outset of chemotherapy treatment, though evidently, without neglecting the other two groups.

We also found that patients with more severe adverse effects manifested worse physical QoL, as well as fewer positive emotions and more negative emotions. Efforts are required to strengthen the coordination of interdisciplinary teams and consolidate the role of specialized cancer nurses in the assessment and follow-up of cancer patients undergoing outpatient adjuvant chemotherapy, from a comprehensive perspective that helps them improve their self-management, as well as mitigate negative emotions and maintain or increase positive emotions and, consequently, their perceived QoL. In this context, it would be interesting to identify nurse-led

interventions that have proven to be effective and to seek to create a consensus in the care and follow-up of cancer patients undergoing chemotherapy treatment.

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# TABLE LEGENDS

Table 1. Sociodemographic and clinical characteristics of participants overall and by cancer site.

Table 2. Outpatient adjuvant chemotherapy regimens by cancer site.

Table 3. Assessment of quality of life and affect at the start (T1) and end (T2) of chemotherapy adjusted for sex and age, stratified by cancer site: Comparisons of differences and effect sizes.

# FIGURE LEGENDS

Figure. Flow of participants through the study.