

Research Article

Fatigue, Physical Symptoms, Psychological Distress, and Use of Integrative Medicine in Patients With Advanced Cancer

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Fatigue is a significant challenge for cancer patients, substantially affecting their quality of life, physical symptoms, and psychological distress. This study examined the relationship between fatigue in patients with advanced cancer and sociodemographic, clinical, and psychological factors. Conducted across 15 oncology departments in Spain, the study included patients with locally advanced, unresectable, or metastatic cancer eligible for systemic treatment. Participants completed the Fatigue Assessment Scale (FAS), European Organisation for Research and Treatment (EORTC QLQ-C30), Locus of Control (UWBHS), and Brief Symptom Inventory (BSI). A total of 512 patients are participated, classified into low-fatigue (55%) and high-fatigue (45%) groups. High fatigue was associated with lower educational attainment (53% vs. 44%), locally advanced disease (26% vs. 17%), poorer functional status according to ECOG (70% vs. 30%), and shorter expected survival (< 18 months: 51% vs. 37%). Additionally, patients with high fatigue reported greater use of integrative medicine (24% vs. 14%, $p = 0.003$) and higher prevalence of symptoms such as pain, nausea, and memory problems ($p < 0.05$). They also exhibited poorer quality of life and higher psychological distress. These findings highlight the need to develop multidimensional strategies that address both physical symptoms and quality of life to enhance the well-being of cancer patients. Clinically, systematic screening for fatigue and psychological distress, alongside tailored supportive interventions, should be embedded in routine care to optimize outcomes in advanced cancer patients.

Keywords: advanced cancer; fatigue; integrative medicine; psychological distress; quality of life

1. Introduction

Fatigue is a multifaceted and widespread symptom among cancer patients, particularly those undergoing treatment for advanced cancer [1]. Cancer-related fatigue refers to

a persistent sense of physical and/or mental exhaustion that limits daily functioning. It is among the most prevalent symptoms in oncology, affecting 40%–90% of patients during the course of illness [2, 3]. While some degree of fatigue is expected as part of the cancer experience, severe or

persistent fatigue has been associated with a decreased quality of life, reduced functional capacity, and poorer treatment adherence [3, 4]. Additionally, it is linked to a higher prevalence of physical symptoms, psychological distress—including depression and anxiety—and increased utilization of healthcare services [5, 6].

The factors contributing to fatigue in cancer patients are diverse and multifactorial. Sociodemographic variables—age, gender, educational background, and employment—have been consistently linked to fatigue, although results remain heterogeneous [6–8]. For instance, older patients may experience higher levels of fatigue due to lower physical reserve; in contrast, findings regarding gender differences in fatigue levels remain inconclusive. While some studies suggest that women experience greater fatigue than men, possibly due to hormonal, psychological, and distress perception differences [9, 10], others report no significant differences [11]. Low educational attainment and unemployment have also been associated with increased fatigue, potentially due to limited access to symptom relief resources and support systems [12].

Clinical factors such as cancer stage, functional status, and prognosis have also been investigated. Fatigue severity has also been associated with functional impairment as measured by Eastern Cooperative Oncology Group (ECOG) and with reduced life expectancy in advanced cancer [5, 9]. Symptom burden, including pain, nausea, and sleep disturbances, further exacerbates fatigue, creating a vicious cycle that affects overall well-being [3, 4]. These symptoms often coexist and interact, complicating efforts to effectively address fatigue in oncology settings.

Psychosocial factors also play a fundamental role in fatigue among cancer patients [10]. Higher levels of psychological distress, including anxiety and depression, have been shown to strongly correlate with fatigue [10, 11]. Additionally, locus of control can significantly influence the perception and management of fatigue. For instance, an external locus of control, in which the patient perceives they have no control over their situation, can exacerbate both physical and psychological symptoms by increasing feelings of helplessness and dependency while reducing motivation to cope with the situation [12, 13]. This perceived lack of control, combined with the absence of adequate care resources, may intensify fatigue, particularly in highly dependent patients [13, 14].

Alongside these well-established psychosocial and clinical correlates, some patients turn to integrative medicine practices such as acupuncture, meditation, or other complementary therapies when experiencing high levels of fatigue. Although the evidence supporting these approaches remains limited, their use may reflect patients' efforts to regain a sense of control and to cope with the multidimensional burden of symptoms [15, 16]. In the present study, we included integrative medicine as a secondary variable of interest, while maintaining our primary focus on sociodemographic, clinical, and psychological predictors of fatigue.

Although fatigue has been extensively investigated in early-stage cancer, its correlates in advanced disease remain underexplored, particularly regarding the interplay of

sociodemographic, clinical, and psychosocial factors. To address this gap, the present study analyzed these variables in relation to fatigue profiles among patients with advanced cancer. In addition, it provides novel insights by examining the understudied role of integrative medicine in this population.

2. Materials and Methods

2.1. Study Design and Population. From February 2020 to May 2024, a cross-sectional study was conducted across 15 medical oncology units in various Spanish university hospitals. The study included adult patients aged 18 years or older with a histopathologically confirmed diagnosis of unresectable advanced cancer, who were ineligible for surgical or curative interventions and were candidates for systemic anticancer treatments.

Exclusion criteria encompassed individuals with physical or mental conditions identified by the oncologist as hindering participation. To ensure consistency, oncologists were trained through online meetings with the study coordinators to exclude patients whose sociodemographic or clinical circumstances could compromise their understanding of the study or their ability to participate reliably. Patients who had undergone treatment for another advanced cancer within the past 2 years, or those experiencing significant medical, social, familial, or personal challenges that could interfere with the study, were also excluded. This included patients with cognitive impairments, substantial health deterioration, or those unable to comprehend or complete the study questionnaires. Recruitment was conducted during the initial oncology consultation, during which patients were informed about their diagnosis, disease stage, and available systemic treatments. Participants who agreed to join the study provided written informed consent and received questionnaires to complete and return at their next visit.

The study was approved by the Ethics Review Committee of each participating hospital as well as the Spanish Agency of Medicines and Health Products (AEMPS; identification code: ES14042015). Participation was voluntary, anonymous, and ensured no disruption to patients' standard care. Out of 547 individuals initially recruited, 512 met the eligibility criteria. Thirty-five participants were excluded for various reasons: 9 did not meet the inclusion criteria, 9 met at least one exclusion criterion, and 17 provided incomplete data.

2.2. Variable Description. Sociodemographic and clinical data were collected from patients participating in the study, including sex (male or female), age (≤ 65 years or > 65 years), marital status (married or in a relationship vs. single), educational level, and employment status (unemployed or employed).

Regarding clinical data, tumor location (bronchopulmonary, colorectal, pancreas, breast, stomach, or other), histology (adenocarcinoma or other), disease stage (locally advanced or with distant metastases), type of treatment

received (chemotherapy, immunotherapy, targeted functional therapies, or other), ECOG performance status (0 or 1 vs. 2 or higher), and estimated survival (<18 months or ≥ 18 months) were recorded. This information was uniformly obtained from all participating hospitals as part of the study protocol. Data were managed by medical oncologists through a centralized digital platform.

Three months after the initiation of systemic treatment, when toxicities such as fatigue are often most evident and treatment decisions are reassessed, patients were asked to complete the Fatigue Assessment Scale (FAS), the European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30), the Locus of Control (UWBHS), and the Brief Symptom Inventory (BSI). In addition, they were asked whether they had used any integrative therapies and, if so, to specify the type, including homeopathy, mind-body approaches (e.g., yoga, meditation, coaching), biological therapies, body-based methods (massage, chiropractic), acupuncture, and energy-based therapies (tai chi, Reiki).

Fatigue was assessed with the 10-item FAS, which covers both physical and mental aspects but has been validated as a unidimensional measure of overall fatigue [17]. Items are rated on a 5-point Likert scale (10–50 total score), with higher values indicating greater severity [18]. The Spanish version has shown good reliability and validity [19].

Quality of life was measured with the EORTC QLQ-C30, a widely used 30-item questionnaire in oncology. It provides three main indices: functional status (physical, role, emotional, social, and cognitive functioning), symptom burden (pain, fatigue, nausea, sleep problems, appetite loss, among others), and global health status. Scores are standardized from 0 to 100, with higher values reflecting better functioning or health, or greater symptom severity depending on the subscale. The questionnaire has been validated across multiple tumor types, shows strong internal consistency, requires less than 15 min to complete, and has a validated Spanish version [20].

Perceived control was measured with the Locus of Control Scale (UWBHS), which captures internal versus external illness-related control beliefs [21]. Higher externality scores reflect a perception that outcomes are determined by others or external circumstances. The UWBHS has been validated across diverse populations and has shown significant associations with psychological outcomes [21].

Psychological distress was assessed using the BSI-18, which screens for anxiety, depression, and somatization [22]. Items are rated on a 5-point Likert scale, yielding both subscale scores and a Global Severity Index, with higher scores reflecting greater psychological distress. The Spanish version of the BSI has been validated for its reliability and validity [23].

2.3. Statistical Methods. Descriptive statistics and frequency distributions were calculated to summarize demographic and clinical characteristics. A cluster analysis was performed to identify participants with similar fatigue patterns. Clustering variables included the fatigue items, and participants with any missing FAS scores were excluded, as this

technique requires complete data for all variables. The k-means method was used with Euclidean distances between observations to estimate clusters, along with Ward's hierarchical clustering method, which defines the distance between two clusters based on the squared error criterion [24]. In all cases, distances were computed from raw data to incorporate the elevation, scatter, and shape of patients' profiles [25]. The optimal two-cluster solution was determined based on dendrogram inspection, silhouette index values, and clinical interpretability, distinguishing between low and high fatigue. Analyses of variance (ANOVA) and chi-square tests were conducted to examine differences in demographic, clinical, and psychological characteristics between the fatigue profiles. Eta-squared ranges between 0 and 1, with $\eta^2 \sim 0.01$ indicating a small, $\eta^2 \sim 0.06$ a medium, and $\eta^2 > 0.14$ a large effect size [25]. Statistical significance was set at a p -value of < 0.05 . All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) software, Version 26.0 (IBM SPSS Statistics for Windows, Armonk, NY, USA: IBM Corp.).

3. Results

3.1. Sociodemographic and Clinical Characteristics. The demographic and clinical characteristics of the 512 study participants, categorized into low fatigue (55%, $n = 280$) and high fatigue (45%, $n = 232$) groups, are summarized in Table 1. The cluster analysis identified two distinct profiles: a low-fatigue group ($M = 21.41$, $SD = 2.38$) and a high-fatigue group ($M = 24.83$, $SD = 7.16$). Significant differences were identified in educational level, disease stage, ECOG performance status, and estimated survival. Participants with lower educational attainment (primary education) were more likely to report high fatigue (53%) compared to low fatigue (44%) ($p = 0.042$). Similarly, those with locally advanced disease showed higher levels of fatigue (26%) compared to participants with metastatic disease (17%) ($p = 0.016$). ECOG performance status was strongly associated with fatigue profiles, with participants reporting high fatigue more frequently having ECOG scores of 2 or higher (70%) compared to those in the low-fatigue group (30%) ($p = 0.001$). Furthermore, an estimated survival of less than 18 months was significantly associated with high fatigue (51% vs. 37%, $p = 0.001$).

Other variables, such as sex, age, marital status, employment, tumor site, histology, and type of treatment, did not show significant differences between fatigue groups ($p > 0.05$). These results underscore the impact of clinical and prognostic factors on fatigue, highlighting the importance of performance status and disease progression in understanding fatigue profiles among oncology patients.

3.2. Integrative Medicine Use and Symptoms Among Oncology Patients With Different Fatigue Levels. The use of integrative medicine and the prevalence of symptoms among the fatigue profiles are presented in Table 2. Participants in the high-fatigue group were more likely to report the use of integrative medicine (24%) compared to those in the low-

TABLE 1: Differences in demographic and clinical characteristics among the fatigue profiles ($n = 512$).

Variable	Total n (%) 512 (100%)	Low fatigue n (%) 280 (55%)	High fatigue n (%) 232 (45%)	X^2	p -value
Sex					
Male	286 (56)	161 (57)	125 (54)	0.675	0.411
Female	226 (44)	119 (43)	107 (46)		
Age					
≤ 65 years	204 (40)	103 (37)	101 (44)	2.411	0.120
> 65 years	308 (60)	177 (63)	131 (56)		
Marital status					
Married or partnered	361 (70)	191 (68)	169 (73)	1.303	0.254
Not partnered	151 (30)	89 (32)	63 (27)		
Educational level					
Primary	244 (48)	122 (44)	122 (53)	4.133	0.042
High school or more	268 (52)	158 (56)	110 (47)		
Employment					
Unemployed	298 (58)	162 (58)	137 (59)	0.075	0.785
Employed	214 (42)	118 (55)	95 (41)		
Tumor site					
Bronchopulmonary	144 (28)	77 (28)	67 (29)	6.721	0.242
Colorectal	98 (19)	62 (22)	36 (16)		
Pancreas	50 (10)	21 (8)	28 (12)		
Breast	69 (14)	37 (13)	32 (14)		
Stomach	27 (5)	17 (6)	10 (4)		
Others	124 (24)	66 (24)	59 (25)		
Histology					
Adenocarcinoma	348 (68)	195 (70)	154 (66)	0.623	0.430
Others	164 (32)	85 (30)	78 (34)		
Stage					
Locally advanced	108 (21)	48 (17)	60 (26)	5.795	0.016
Dis. metastases (IV)	404 (79)	232 (83)	172 (74)		
Type of treatment					
Chemotherapy	245 (48)	130 (46)	115 (50)	1.469	0.832
Immunotherapy	32 (6)	19 (7)	13 (6)		
Targeted therapies	31 (6)	16 (6)	15 (7)		
Others	204 (40)	115 (41)	89 (38)		
ECOG					
0 or 1	302 (59)	139 (50)	69 (30)	20.147	0.001
2 or more	210 (41)	138 (50)	158 (70)		
Estimated survival					
< 18 months	208 (41)	104 (37)	119 (51)	10.333	0.001
≥ 18 months	296 (59)	176 (63)	113 (49)		

fatigue group (14%) ($p = 0.003$). Details of the specific modalities are summarized in Table 3, showing that the most commonly reported practices were homeopathy (26%) and mind-body approaches such as yoga, meditation, or coaching (26%), followed by biological therapies (19%), body-based methods (15%), acupuncture (10%), and energy-based therapies such as tai chi or Reiki (4%).

Symptom prevalence was notably higher among participants in the high-fatigue group across nearly all categories. High fatigue was significantly associated with higher rates of pain (71% vs. 44%, $p = 0.001$), nausea/vomiting (51% vs. 20%, $p = 0.001$), diarrhea (44% vs. 35%, $p = 0.043$), skin problems (53% vs. 39%, $p = 0.001$), infections (29% vs. 8%, $p = 0.001$), and memory issues (72% vs. 29%, $p = 0.001$). Other symptoms significantly more common in the high-fatigue group included thyroid-related problems (21% vs. 9%, $p = 0.001$), sores (47% vs. 28%, $p = 0.001$), liver

issues (32% vs. 16%, $p = 0.001$), kidney problems (25% vs. 11%, $p = 0.001$), and patient-reported scarring (63% vs. 50%, $p = 0.002$). A small but significant difference was also observed in patient death rates, with a higher proportion in the high-fatigue group (6%) compared to the low-fatigue group (3%) ($p = 0.042$). These findings highlight the complex interplay between symptom burden and fatigue levels in oncology patients, suggesting a potential role for integrative medicine in addressing these challenges.

3.3. Psychosocial Characteristics Related to Patients' Fatigue Profiles. When examining the relationships between fatigue profiles and psychosocial characteristics using the scales (EORTC, UWBHS, BSI), significant differences were observed between the low-fatigue ($n = 280$) and high-fatigue ($n = 232$) groups. Participants in the high-fatigue group reported lower functional quality of life ($M = 49.3$ vs.

TABLE 2: Differences in the use of integrative medicine in oncology among the fatigue profiles ($n = 512$).

Variable	Total n (%) 512 (100%)	Low fatigue n (%) 280 (55%)	High fatigue n (%) 232 (45%)	χ^2	p -value
Medicine integrative					
No	407 (82)	236 (86)	171 (76)	9.014	0.003
Yes	91 (18)	37 (14)	54 (24)		
Symptoms					
Fever	70 (14)	24 (9)	46 (20)	13.502	0.001
Pain	288 (56)	123 (44)	165 (71)	37.641	0.001
Loss of appetite	276 (54)	107 (38)	169 (73)	60.675	0.001
Nausea/vomiting	175 (34)	57 (20)	118 (51)	52.095	0.001
Diarrhea	198 (39)	97 (35)	101 (44)	4.103	0.043
Skin problems	231 (45)	108 (39)	123 (53)	10.468	0.001
Infections	89 (17)	22 (8)	67 (29)	38.815	0.001
Scars	285 (56)	138 (50)	147 (63)	9.921	0.002
Thyroid	74 (15)	25 (9)	49 (21)	15.124	0.001
Sores	187 (37)	77 (28)	110 (47)	21.435	0.001
Liver	119 (23)	44 (16)	75 (32)	19.438	0.001
Kidney	88 (17)	30 (11)	58 (25)	18.037	0.001
Memory	249 (49)	82 (29)	167 (72)	91.975	0.001
Patient's death	21 (4)	7 (3)	14 (6)	4.140	0.042

TABLE 3: Types and frequencies of integrative medicine modalities used by patients ($n = 91$).

Modality	n	%
Homeopathy	24	26
Mind-body approaches (yoga, meditation, coaching)	24	26
Biological therapies	17	19
Body-based methods (massage, chiropractic)	14	15
Acupuncture	9	10
Energy-based therapies (tai chi, Reiki)	4	4

$M = 72.5$; $\eta^2 = 0.372$), higher symptom burden ($M = 38.8$ vs. $M = 16.8$; $\eta^2 = 0.290$), and worse overall health status ($M = 47.3$ vs. $M = 57.3$; $\eta^2 = 0.039$).

Additionally, those in the high-fatigue group scored significantly lower on locus of control ($M = 15.4$ vs. $M = 16.6$; $\eta^2 = 0.018$) and reported greater psychological distress ($M = 70.6$ vs. $M = 62.4$; $\eta^2 = 0.312$). These findings highlight the considerable psychosocial disparities associated with fatigue levels in cancer patients (Table 4).

4. Discussion

Fatigue is highly prevalent in oncology and has substantial consequences for daily functioning, treatment adherence, and overall quality of life [1]. This study explored sociodemographic, clinical, and psychosocial factors associated with fatigue, classifying participants into low- and high-fatigue profiles. The findings partially support the influence of variables such as educational level, disease stage, functional status, and overall health. Whereas most research has focused on early-stage cancer, our study sheds light on fatigue in advanced disease, revealing distinct patterns and providing clinically meaningful contributions to an underexplored area.

In this study, patients with high fatigue not only reported higher levels of psychological distress but also showed

a greater tendency to use integrative medicine (24% vs. 14%). This suggests that while distress is a central correlate and should be addressed primarily through evidence-based psychological interventions, some patients additionally seek complementary approaches to cope with their symptoms and improve quality of life. This finding is consistent with meta-analyses indicating that more than half of cancer patients experience fatigue, a prevalence significantly higher than that observed in the general population and individuals with other diseases [26, 27]. In our study, participants with only primary education reported higher levels of fatigue compared to those with higher education. This aligns with previous studies, such as Schmidt et al. [28] in breast cancer, where fatigued patients had lower educational attainment, and Wang et al. [29] in colorectal cancer, which showed better fatigue management among patients with university education. These findings suggest that lower educational levels may limit access to or understanding of information on symptom management, exacerbating fatigue.

Disease stage also influenced the perception of fatigue. Participants with locally advanced disease reported higher fatigue levels compared to those with metastatic disease. Although this result may seem counterintuitive, it could be explained by several factors. Patients with metastatic disease, facing a worse prognosis, may receive less aggressive palliative treatments and have had more time to psychologically adapt to their diagnosis and develop coping strategies. On the other hand, patients with locally advanced disease are often undergoing more active and intensive treatment, which leads to more severe side effects and greater uncertainty about the disease course, potentially increasing the perception of fatigue. These results are similar to those found by other authors, who have observed that disease progression can directly influence the intensity of fatigue [30, 31].

The ECOG performance status was strongly associated with fatigue, with higher ECOG scores (≥ 2) being more

TABLE 4: Differences in psychosocial characteristics and fatigue profiles.

	Low fatigue <i>n</i> (%) 280 (55%)		High fatigue <i>n</i> (%) 232 (45%)		<i>F</i>	<i>p</i>	Eta-squared
	Mean	SD	Mean	SD			
Quality of Life (EORTC)							
Functional scale	72.5	11.9	49.3	18.1	296.87	0.001	0.372
Symptom scale	16.8	13.1	38.8	20.6	205.25	0.001	0.290
Health status	57.3	28.5	47.3	19.7	20.18	0.001	0.039
Locus of Control (UWBHS)	16.6	4.4	15.4	3.8	9.12	0.03	0.018
Psychological distress (BSI)	62.4	5.3	70.6	6.9	228.08	0.001	0.312

Note: UWBHS, Locus of Control.
Abbreviations: BSI, Brief Symptom Inventory; EORTC, European Organisation for Research and Treatment of Cancer; SD, standard deviation.

frequent in the high-fatigue group. This finding highlights the crucial role of functional status in understanding fatigue. Patients with limited physical functioning often report greater fatigue due to the combined impact of disease burden and reduced capacity for daily activities [28, 31]. Similarly, estimated survival emerged as a significant predictor, as participants with a prognosis of less than 18 months reported higher levels of fatigue. This association may be linked to the psychological distress associated with a shorter life expectancy and the greater physical burden of advanced disease [29]. Fatigue is recognized as a prognostic factor in advanced cancer [32], reducing survival time by approximately 39%–44% [33].

On the other hand, variables such as the type of treatment did not show significant differences between fatigue profiles in our cohort. This lack of association suggests that fatigue may be more strongly influenced by clinical and prognostic factors than by broader demographic characteristics.

In our study, patients with high fatigue showed a greater tendency to use integrative medicine compared to those with low fatigue (24% vs. 14%). Among the most common practices were homeopathy and mind–body approaches, used by 26% of users. Other methods included biological therapies (19%), body-based approaches (15%), acupuncture (10%), and energy-based therapies such as tai chi or Reiki (4%). This increased use of integrative medicine suggests that patients with high fatigue seek complementary approaches to alleviate their symptoms and improve their quality of life, aligning with existing literature on the multidimensional impact of fatigue in cancer care.

Psychological interventions such as cognitive-behavioral therapy, psycho-oncological support, and mindfulness-based programs have demonstrated robust evidence in reducing cancer-related fatigue and distress and should be considered first-line strategies. Several studies support the effectiveness of integrative therapies in managing fatigue, particularly in cancer patients [15, 16]. Digital interventions, such as IM@Home, have been shown to significantly reduce fatigue [34], while holistic approaches like Integrated-pathy have improved quality of life and reduced cancer-related pain [35]. Additionally, mind–body therapies such as mindfulness and exercise have demonstrated benefits for both physical and emotional well-being [36]. However, some patients do not experience sufficient relief with these

methods, underscoring the need for further research to optimize treatments and better understand individual responses [37].

Our findings confirm that fatigue is strongly associated with a higher symptom burden in cancer patients, aligning with previous studies that have identified its relationship with multiple physical symptoms and systemic factors [38]. In our study, patients with high fatigue exhibited significantly higher rates of pain (71% vs. 44%), nausea/vomiting (51% vs. 20%), and memory problems (72% vs. 29%), highlighting its multidimensional impact and the need for a comprehensive approach to its management.

Additionally, the higher incidence of thyroid dysfunction (21% vs. 9%) and infections (29% vs. 8%) in this group suggests that fatigue may be influenced by systemic alterations affecting the patient’s overall health status. Likewise, mortality was higher in the high-fatigue group (6% vs. 3%), suggesting that fatigue could serve as a prognostic marker in disease progression. Recent studies also indicate that severe fatigue is linked to a higher risk of toxicity in cancer treatments, reinforcing its clinical relevance [39].

On the other hand, some studies have suggested that lifestyle-related factors, such as physical activity prior to diagnosis, may mitigate fatigue severity [38]. This underscores the importance of designing personalized interventions that not only address fatigue as a symptom but also consider its underlying causes and modifiable factors to improve patients’ quality of life.

In our study, fatigue showed a significant association with quality of life, health status, and psychological distress. Patients with high fatigue exhibited a notable reduction in functional quality of life and a higher symptom burden. Likewise, this group showed significantly higher levels of psychological distress, as evidenced by elevated scores in anxiety, depression, and somatic symptoms. These findings align with previous studies that have identified a correlation between fatigue and impairment in both physical and psychological domains, such as in hemodialysis patients, where fatigue is associated with a lower quality of life [40], and in cancer survivors, who report significantly reduced quality of life when experiencing severe fatigue [41, 42]. These results underscore the interconnectedness of physical and emotional well-being, suggesting that fatigue not only intensifies symptom burden but also exacerbates psychological distress and compromises overall quality of life. From

a clinical perspective, this highlights the importance of systematically screening for distress in patients with high fatigue and integrating evidence-based psychological support as a core component of fatigue management.

4.1. Limitations. This study has some limitations that should be considered when interpreting the findings. First, patients with different tumor types were included without making comparisons between them, limiting the generalizability of the results to specific metastatic neoplasms. Second, the sample consists exclusively of cancer patients in Spain, a country with universal access to public healthcare, meaning the results may not be directly applicable to healthcare settings with different care models and resources, particularly in non-Western countries. Another limitation is the cross-sectional design, which prevents establishing causal relationships between fatigue, emotional distress, and other clinical factors, or analyzing their evolution over time. Exclusion criteria were based on clinical judgment without standardized tools, which may introduce selection bias and limit representativeness, despite investigators being trained to apply them consistently. Finally, integrative medicine use was considered only as an exploratory variable, and no causal role can be inferred. Fatigue was analyzed dichotomously using an empirical clustering approach, which, while consistent with conventional thresholds, inevitably reduced variability compared with continuous analyses. Assessments were also conducted 3 months after treatment initiation, which may not capture trajectories detectable at other time points. Future longitudinal studies should explore the course of fatigue, psychological distress, and quality of life and directly compare the impact of psychological interventions and complementary therapies to inform clinical practice.

Despite these limitations, the study highlights significant associations between fatigue severity, the use of integrative medicine, and symptom burden in cancer patients. The results indicate that patients with severe fatigue are more likely to turn to integrative approaches such as homeopathy, yoga, and biological therapies, suggesting a potential unmet need for complementary strategies in symptom management. Furthermore, these patients reported a significantly higher prevalence of physical symptoms, including pain, nausea, and memory problems, reinforcing the multidimensional nature of fatigue and its impact on quality of life.

5. Conclusions

From a clinical perspective, these findings emphasize the importance of fatigue as a critical factor in the cancer patient experience. Systematic screening could facilitate the early identification of patients at risk of a high symptom burden and allow for more personalized interventions. Given the strong association between fatigue and psychological distress, evidence-based psychological support should be prioritized in routine care. Complementary therapies may also contribute as useful adjuncts; however, further research is warranted to establish their efficacy, applicability, and role in alleviating symptom-related distress.

Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality restrictions but are available from the corresponding author on reasonable request.

Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki. Approval was obtained from the Research Ethics Committee of the Principality of Asturias (May 17, 2019) and by the Spanish Agency of Medicines and Medical Devices (AEMPS) (identification code: L34LM-MM2GH-Y925U-RJDHQ). The study was observational and non-interventional. All participants provided written informed consent.

Consent

Please see Ethics Statement.

Disclosure

The funders had no role in the design of the study, in the collection, analysis, or interpretation of the data, or in the writing of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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