

# Comorbidities between fatigue and depression in patients with colorectal cancer\*

CO-MORBIDADE FADIGA E DEPRESSÃO EM PACIENTES COM CÂNCER COLO-RETAL

ENFERMEDAD CONCOMITANTE: FATIGA Y DEPRESIÓN EN PACIENTES CON CÁNCER COLON-RECTAL

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## ABSTRACT

The objective of this study was to identify and characterize the comorbidities of fatigue and depression in colorectal cancer patients. A non-probabilistic sample of 154 outpatients (53% men; mean age 49.6±11.7 years; mean education 8.9±5.4 years). Fatigue was evaluated using the Revised Piper Fatigue Scale (min:0; max:10) and depression was evaluated using the Beck Depression Inventory (BDI) (min:0; max: 63). Fatigue was identified by 76 (49.4%) patients, and was intense (total score ≥ 6) for 19.7%. Scores compatible with depression (BDI > 20) were found in 11 (7.1%) patients. Fatigue and depression were correlated ( $r=0.395$ ,  $p<0.001$ ). Comorbidities of moderate/severe fatigue and dysphoria/depression occurred in 12.3%. Fatigue was present in all patients with depression (100%) and depression occurred in 18% of patients with fatigue. Fatigue and depression are related phenomena. Comorbidities can be deleterious to the patient. Depression had a stronger effect on the occurrence of fatigue than the effect of fatigue on depression.

## KEY WORDS

Colorectal neoplasms.  
Fatigue.  
Depression.  
Palliative care.

## RESUMO

O estudo teve como objetivos caracterizar e identificar a comorbidade entre fadiga e depressão em pacientes com câncer colorretal. A amostra não-probabilística foi de 154 pacientes ambulatoriais (53% homens; idade média 49,6±11,7 anos; escolaridade média 8,9±5,4 anos). A fadiga foi avaliada pela Escala de Fadiga de Piper Revisada e o humor pelo Inventário de Depressão de Beck. A fadiga foi relatada por 76 (49,4%) pacientes e foi intensa (escore total ≥ 6) para 19,7% deles. Escores que sugerem depressão (IDB>20) foram encontrados em 11 (7,1%) pacientes. Fadiga e depressão estavam correlacionadas ( $r=0,395$ ;  $p 0,001$ ). A co-morbidade fadiga moderada/intensa e disforia/depressão ocorreu em 12,3%. A fadiga estava presente na totalidade dos doentes deprimidos (100%), e a depressão ocorreu em 18% dos doentes fatigados. Fadiga e depressão são fenômenos relacionados, a sua comorbidade pode ser muito deletéria ao doente; a depressão foi mais importante para a ocorrência de fadiga do que a fadiga para a depressão.

## DESCRIPTORIOS

Neoplasias colorretais.  
Fadiga.  
Depressão.  
Assistência paliativa.

## RESUMEN

El estudio tuvo como objetivos caracterizar e identificar la relación entre la fatiga y la depresión en pacientes con cáncer colon-rectal. La muestra no probabilística fue de 154 pacientes de ambulatorio (53% hombres; edad promedio 49,6±11,7 años; escolaridad promedio 8,9±5,4 años). La fatiga fue evaluada por la Escala de Fatiga de Piper Revisada y el humor por el Inventario de Depresión de Beck. La fatiga fue relatada por 76 (49,4%) pacientes y fue intensa (puntaje total ≥ 6) para 19,7% de ellos. Puntajes que sugieren depresión (IDB>20) fueron encontrados en 11 (7,1%) pacientes. La fatiga y la depresión estaban correlacionados ( $r=0,395$ ;  $p 0,001$ ). La enfermedad concomitante fatiga moderada/intensa y disforia/depresión ocurrió en 12,3%. La fatiga estaba presente en la totalidad de los enfermos deprimidos (100%), y la depresión ocurrió en 18% de los enfermos fatigados. Fatiga y depresión son fenómenos relacionados (concomitantes), y su acción puede ser muy deletérea para el enfermo; la depresión fue más importante para la ocurrencia de fatiga que la fatiga para la depresión.

## DESCRIPTORIOS

Neoplasias colorrectales.  
Fatiga.  
Depresión.  
Atención paliativa.

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## INTRODUCTION

Fatigue and depression are mentioned in international literature as common symptoms in patients with cancer. However, the relationship between them is insufficiently understood, especially in colorectal cancer cases. In Brazil, fatigue and depression occurrence and prevalence in cancer patients are not well known. The evaluation and record of these symptoms are not appropriately taken according to what is inferred by a study on the record of subjective symptoms in this sector<sup>(1)</sup>.

Fatigue occurs in 19 to 99% of patients and its frequency and magnitude vary as the evolution of the oncologic disease<sup>(2-4)</sup>. It regards an unpleasant feeling with physical, psychic and emotional symptoms described as a type of tiredness that is not improved by the usual energy recovery strategies<sup>(5)</sup>. It varies in intensity and duration and reduces, in different grades, the ability of performing daily tasks<sup>(5)</sup>. It is multifactor, impacting various life domains; also, the factors composing it are not yet well-known. Among emotional factors, depression is most studied. It occurs between 1.5 to 57% of cancer patients<sup>(6-7)</sup> and can affect patients at any phase of the disease<sup>(6-7)</sup>.

Fatigue follows humor disorders. Depression is considered a triggering factor for fatigue<sup>(8)</sup>, but the magnitude of this correlation is still not certain. It is described as varying around 0.16 to 0.8<sup>(9)</sup>.

Depression is a humor affection disorder characterized by global organic and psychic alterations, for a minimum period of two weeks, involving depression episodes and at least four of the following symptoms: sadness complaints, hopelessness, loss of general pleasure, loss of appetite, sleep disturbances, psychomotor alterations, energy decrease, feelings of uselessness and guilt, and suicidal thoughts<sup>(10)</sup>. Depression prevalence in colorectal cancer patients occurs in 36.7% of patients<sup>(11)</sup>.

Only a few studies have analyzed the relationship between fatigue and depression in patients with colorectal cancer<sup>(11)</sup> and none have identified comorbidities among the symptoms. These facts have motivated the elaboration of this present study.

## OBJECTIVES

This study has the objective of characterizing and identifying comorbidities between fatigue and depression in colorectal cancer patients.

## METHOD

### *Sample, location and period*

This is a cross-sectional study, with a non-probabilistic sample of 154 patients with primary colon or rectal cancer,

undergoing clinic treatment. At any stage of the disease, age equal or over 18 years old and appropriate capacity to understand and verbalize attained by six years of minimum educational level. Collection was carried out into four oncology services of the city of São Paulo (Cancer Hospital A.C. Camargo, Santa Helena Hospital, Brigadeiro Hospital and Nove de Julho Oncology Clinics), from July of 2006 to June of 2007, after the approval from the Research Ethics Committee of these institutions (Protocol No. 511/2005/REC-EEUSP). All patients who agreed to participate signed a two-copy Free and Informed Consent Form.

### *Procedures and Data Collection Instruments*

Data collection team was composed by the main researcher, three nurses and one nursing graduation student. Collection procedures were standardized and all parties were previously trained with the aim to ensure data impartiality and fidelity.

Patients were forwarded by the oncology services to collectors. After certifying inclusion criteria and they agreed to participate in the research, collectors interviewed the subjects. After signing the Free and Informed Consent Form, they were categorized according to socio-demographic data, from the disease to treatment, functional capacity (Karnofsky's Scale), fatigue (reviewed Piper's Fatigue Scale) and humor (Beck's Depression Inventory – BDI).

Karnofsky's Scale aimed at measuring the functional capacity. In other words, it measures the capability to perform daily life activities. This was an independent variable of this study. In the oncology context, this type of measure is broadly used to determine if the patient can undergo chemotherapy and if there is a need to adjust the dose, for instance. The score varies from 100%, which indicates full health, to 0%, which indicates death. Despite its broad use, there is no acknowledgment of a study where its psychometric properties were tested in Brazilian culture<sup>(12)</sup>.

The Reviewed Piper's Fatigue Scale is a multi-dimensional self-report instrument, validated for the Brazilian culture<sup>(13)</sup>. The Brazilian version was validated with 584 patients with various cancer types and 373 healthy individuals (184 companions and 189 nursing graduation students). Reliability of this instrument to the sample of this study was very high (Cronbach  $\alpha=0.94$ ) and dimensions were confirmed by factor analysis. The instrument has 22 items and 3 dimensions (behavioral/intensity - 6 items, affective - 5 items and sensitive/cognitive and emotional - 11 items). Total and dimensional score vary from 0 to 10. Cutting points were established according to score distribution in percentage of the sample. Twenty-five percent referred to 3, fifty percent referred to 4.8 and 75% referred to 6.2. Score 0 represented no fatigue, scores less than 3 indicated light fatigue, scores equal to 3 and lower than 6 indicated mild fatigue, and scores equal to or higher than 6, indicated intense fatigue.

Fatigue follows humor disorders. Depression is considered a triggering factor for fatigue.

The Beck's Depression Inventory was validated for the Brazilian culture<sup>(14)</sup>. It is composed of 21 items graduated from 0 to 3; minimum score is 0 (no depression) and maximum score is 63 (maximum depression). Cutting points adopted for populations with no previous depression diagnosis are: scores between 0 and 15 define absence of depression, scores between 16 and 20 show dysphoria and scores higher than 20 are compatible to depression. The reliability tested in this present study was good (Cronbach  $\alpha=0.83$ ).

### Data analysis

Data were organized into Excel® spreadsheets and statistics tests were carried out using SPSSv.15.0 software. Comorbidities were identified under absolute and relative fre-

quency. The correlation between fatigue and depression scores was evaluated by the Spearman correlation coefficient. Although studies show the relationship between fatigue and/or depression and the characterization variables of the samples used in this study (socio-demographic, disease and treatment), they were not evaluated since they went beyond this study's objectives.

## RESULTS

In Table 1, the sample characteristics are presented. There was a predominance of colon cancer individuals, patients with stage IV tumors and of patients undergoing chemotherapy. Functionality was being maintained in 80% of patients.

**Table 1** - Patients distribution (n=154) according to socio-demographic, disease and treatment characteristics - São Paulo - 2007

Socio-Demographic Data		N	%
Gender	Male	82	53.2
Age	Mean (SD)	59.9 (DP=11.7)	
	Median (Variance)	60 (28-84)	
Marital Status	Married	104	67.5
Education (in years)	Mean (SD)	10.7 (DP=5.4)	
	Median (Variance)	11 (0-26)	
Income per capita (USD\$) US\$ 1.00 = R\$ 2.00 reais	Mean (SD)	1,624.06 (DP=1,811.67)	
	Median (Variance)	1,062.50 (83-12,000)	
Treatment and Disease Data			
Primary Tumor Location	Colon	108	70.1
	Rectal	46	29.9
Stage*	I	5	3.2
	II	17	11.0
	III	16	10.4
	IV	34	22.1
	No data	82	53.3
Performance Status (Karnofsky's Scale)	100% - 80%	123	79.9
	70% - 60%	25	16.2
	50%	2	1.3
	No data	4	2.6
Current treatments	Chemotherapy	94	61.1
	Radiotherapy	1	0.6
	Chemotherapy + Radiotherapy	2	1.3
	Hormones Therapy	1	0.6
	Not under treatment	56	36.4

\*Stages were described by the TNM system according to the oncologist's description in the patient's medical file

Table 2 presents the intensity of fatigue and depressive symptoms. Fifty percent of patients presented fatigue, where one-fifth of these were intense. Depression was ob-

served in 7% of patients, however, some humor alteration was reported by 16.2% of the cases.

**Table 2** - Presence and intensity of fatigue and depression in colorectal cancer patients - São Paulo - 2007

		N	%
<b>Fatigue (n=154)</b>	Yes	76	49.4
	No	78	50.6
<b>Fatigue (n=76)</b>			
Mean=4.5 (SD=1.8)	Light (<3)	15	19.7
Median=4.4	Mild (≤3 or <6)	46	60.5
Variation (1.1 to 9.6)	Intense (6 ≥ 10)	15	19.7
<b>Depression (n=154)</b>			
Mean=9.4 (SD=7.1)	Absence of Depression (0-15)	129	83.8
Median=9.0	Dysphoria (16 - 20)	14	9.1
Variation (0 to 37)	Depressive Symptoms (21 - 63)	11	7.1

Table 3 presents fatigue and depression comorbidities. The correlation between fatigue and depression was positive, mild and statistically significant ( $r=0.395$ ;  $p<0.01$ ). Around 4.5% of patients presented intense fatigue and de-

pression comorbidities; in 7.1% of the cases, mild/intense fatigue and depression comorbidities were observed and in 12.3% of the cases mild/intense fatigue and dysphoria/ depression were observed.

**Table 3** - Fatigue and depression in colorectal cancer patients - São Paulo - 2007

		Reviewed Piper's Fatigue Scale			
		No fatigue (n=78)	Light Fatigue (n=15)	Mild Fatigue (n=46)	Intense Fatigue (n=15)
<b>Beck's Depression Inventory</b>	No depression (n=129)	75	12	38	4
	Dysphoria (n=14)	3	3	4	4
	Depression (n=11)	0	0	4	7*
<b>Depression scores X Fatigue scores</b> Spearman Test $r=0.395$ $p<0.01$					

\* Comorbidities

In patients with depression (n=11), 64% reported intense fatigue; among patients with intense fatigue (n=15), 46.7% presented depression. In patients that showed no depression (n=129), 3.1% presented intense fatigue and in patients with no fatigue (n=78) none had depression (Table 3).

## DISCUSSION

The study demonstrated that fatigue and depression were positively correlated, occurring in comorbidities and were frequent among patients. Isolated fatigue and depression can cause limitations and it can also be even more deleterious, increase physical, emotional and social incapacity, compromising treatment adherence and causing considerable suffering to patients and their family. Few

studies, worldwide, analyzed the relations and comorbidities between fatigue and depression in colorectal cancer patients. Nationally, this is the first study.

Approximately half of the sample had experienced some degree of fatigue (49.4%) and in 39.6% it was mild and intense (Table 2). This prevalence was superior compared to the one found in colorectal cancer patients and colorectal cancer survivors<sup>(15-16)</sup> and inferior to the study that evaluated fatigue in colorectal cancer patients one year after diagnosis<sup>(17)</sup>.

Possibly, results discrepancy regards the different health/sickness conditions and patients' personal characteristics. In this present research, the mean age was 60 years old. Most patients had a good educational level and

preserved functionality. All patients were undergoing clinical treatment. Few studies evaluated the relation between fatigue and/or depression and socio-demographic variables as gender, age, educational level, marital status, working activity, income *per capita*, and color of skin. They all demonstrated contradictory and inconclusive results. In addition to cancer treatments, risk or predicting factors for symptoms appearance<sup>(13)</sup> and the disease stage also influence the prevalence of fatigue and depression. This present study did not evaluate the relationship between fatigue and/or depression and the characterizing variables of the sample.

The reviewed Piper's Fatigue Scale, used in this study, demonstrated good reliability. Despite its median extension (22 items), it did not present fulfilling difficulties. Among the analyzed results, fatigue was evaluated by various instruments *Fatigue Severity Scale*, *Fatigue Questionnaire*, the *Cancer Fatigue Scale* and the *Bidimensional Fatigue Scale*, *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire* (EORTC-QLQ core 30) and the *Profile of Mood States Scale* (POMS). Different evaluation methods can lead to different results limiting results comparison.

Depression was observed in 7.1% of patients and dysphoria in 9.1%. Depression prevalence was slightly superior to the one found in general Brazilian population (2% to 6%)<sup>(13)</sup>. A similar result to what was observed in studies involving patients with different types of cancer and survivors of Hodgkin's Lymphoma (8% to 3%)<sup>(4)</sup> and inferior to studies on patients under palliative care (35%) and in patients with colorectal cancer (36.7%)<sup>(11)</sup>. These differences can be a result from sample differences and different methods and diagnoses. The Beck's Depression Inventory used in this study was extensively validated in clinical and Brazilian population samples. It demonstrated high reliability for this sample. The Hospital Anxiety and Depression Scale (HADS) was the most used evaluation scale for depression in the studies analyzed here.

A positive and mild correlation was observed between fatigue and depression ( $r=0.395$ ,  $p=0.001$ ) and no study was found that analyzed this correlation in patients with colorectal cancer. Studies involving patients with other types of cancer found superior correlations that varied between  $r=0.55$  and  $r=0.75$ <sup>(3)</sup>. Only one study did not find a statistically significant correlation between fatigue and depression ( $r=0.16$ )<sup>(2)</sup>. A similar result was found in a study on patients with Hodgkin's Lymphoma<sup>(4)</sup>.

Fatigue and depression are related to the worsening of quality of life and in comorbidities, they can be even more deleterious. Comorbidities between fatigue and depression found in this present study were significant: moderate/intense fatigue and dysphoria/depression comorbidities were observed in 12.3% of patients, moderate/intense fatigue and depression comorbidities in 7.1% and intense fatigue and depression in 4.5% (Table 3). A study involving

52 patients with various types of neoplasm found superior comorbidities (19.2%) to this present study<sup>(18)</sup>.

Fatigue is a symptom of a depressive condition and also an item of Beck's Depression Inventory. Among the 154 patients evaluated in the present study, 64.3% have reported some degree of fatigue. In Piper's Fatigue Scale, 14.3% of patients reported some degree of depression. These data suggest fatigue as one of the elements for depression more than depression as one of the elements for fatigue. This analysis is also ensured by the findings in the present study where in patients with depression ( $n=11$ ), 64% reported intense fatigue, and from intense fatigue patients ( $n=15$ ), 46.7% presented depression.

From subjects with moderate/intense fatigue ( $n=61$ ) 18% presented depression and from the depressed patients ( $n=11$ ), 100% presented moderate/intense fatigue. In patients with no depression ( $n=129$ ), 58.1% showed no fatigue and from patients with no fatigue ( $n=78$ ), 96.2% showed no depression (Table 3). These data are unpublished in literature and confirm two distinct phenomena.

Various studies on prostate, breast cancer, hematologic tumors and other solid tumor patients have observed that fatigue damaged their daily life activities, sexuality, quality of life, and that it was positively related to anxiety, depressive symptoms and sleep disorders<sup>(2,18)</sup>. Depression has resulted in the worsening of physical performance, higher somatic complaints, higher anxiety and feelings of insecurity in inter-personal contacts and lower levels of vitality<sup>(18)</sup>.

A few limitations in this present study are mentioned. The sample was non-probabilistic avoiding generalizations and contemplating only clinics treatment patients, excluding colorectal cancer patients admitted to the hospital. The fact may have disguised some differences. These limitations should be overcome in new studies.

The present research contributes for the increase and understanding over the association of fatigue and depression comorbidities in colorectal cancer patients, and also for the understanding of concepts differences between the two phenomena.

## CONCLUSION

Fatigue, although frequent is not well understood, limiting the appropriate care for patients. High prevalence of fatigue was observed (49.4%), low prevalence of depression (7.1%) and moderate positive correlation between fatigue and depression ( $r=0.395$ ,  $p<0.001$ ). Comorbidities between fatigue and depression, under different magnitudes, vary between 4.5% and 12.3%. Findings suggest fatigue as more important for the existence of depression than depression as a composer of fatigue. They are, therefore, two distinct phenomena.

In this context, nurses' actions should minimize symptoms and occurring damages. They regard establishing strat-



egies to identify and control fatigue and depression that are still part of our environment, such as physical activities, alternate sleep and rest, educational programs and cognitive behavioral actions.

This study is pioneer in our sector and fatigue and depression comorbidities in colorectal cancer patients are an internationally innovative result.

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