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ORIGINAL ARTICLE

Influence of depression on survival of colorectal cancer patients drawn from a large prospective cohort

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Abstract

Objective: The prevalence of depressive symptoms immediately after the diagnosis of colorectal cancer (CRC) is high and has important implications both psychologically and on the course of the disease. The aim of this study is to analyse the association between depressive symptoms and CRC survival at 5 years after diagnosis.

Methods: This multicentre, prospective, observational cohort study was conducted on a sample of 2602 patients with CRC who completed the Hospital Anxiety and Depression Scale (HADS-D) at 5 years of follow-up. Survival was analysed using the Kaplan–Meier method and Cox regression models.

Results: According to our analysis, the prevalence of depressive symptoms after a CRC diagnosis was 23.8%. The Cox regression analysis identified depression as an

independent risk factor for survival (HR = 1.47; 95% CI: 1.21–1.8), a finding which persisted after adjusting for sex (female: HR = 0.63; 95% CI: 0.51–0.76), age (>70 years: HR = 3.78; 95% CI: 1.94–7.36), need for help (yes: HR = 1.43; 95% CI: 1.17–1.74), provision of social assistance (yes: HR = 1.46; 95% CI: 1.16–1.82), tumour size (T3–T4: HR = 1.56; 95% CI: 1.22–1.99), nodule staging (N1–N2: HR = 2.46; 95% CI: 2.04–2.96), and diagnosis during a screening test (yes: HR = 0.71; 95% CI: 0.55–0.91).

Conclusions: There is a high prevalence of depressive symptoms in patients diagnosed with CRC. These symptoms were negatively associated with the survival rate independently of other clinical variables. Therefore, patients diagnosed with CRC should be screened for depressive symptoms to ensure appropriate treatment can be provided.

KEYWORDS
colorectal cancer, depression, mental health, mortality, oncology, psycho-oncology, survival

1 | BACKGROUND

Depression is an important public health problem worldwide due to its high prevalence[1] and the disability[2] it generates. Individuals with chronic diseases are twice as likely to develop depression[3,4]; indeed, the rate of depression among individuals with cancer is 49%.[5]

The impact of a cancer diagnosis and treatment has important psychological implications on patients and their families because of the life-threatening nature of this disease.[6] Knowing that a disease could be fatal together with the physical effects produced by the cancer and its treatment are major stressors that can generate symptoms of depression,[7] which entails an additional treatment burden that threatens disease management and control,[5,8] therapeutic compliance,[8] length of hospital stay[9,10] and ultimately, the survival rate.[11,12] Specifically, colorectal cancer (CRC) is a type of cancer that entails different stressors and treatment strategies as well as different factors associated with the impact of the diagnosis.[13,14] Screening and follow-up tests such as a colonoscopy or a barium enema are invasive and generate stress. Moreover, a colectomy, the use of a colostomy and multimodal treatments are all associated with adverse effects for patients. They represent another source of stress that can sometimes result in depressive symptoms after a confirmatory diagnosis, which may have a negative effect on survival.

Surviving cancer is associated with significant emotional distress. Various meta-analyses have detected a significant relationship between depressive symptoms and cancer survival[13,14] and recent studies have provided more evidence that supports this relationship.[4,15,16] These works report that patients with cancer are at greater risk of depression than the general population, though few studies have analysed if a decrease in depressive symptoms is associated with later survival. Giese-Davis et al. (2011)[17] investigated this issue and found that an effective intervention for symptoms of depression was predictive of increased survival (53.6 months) at 14 years in a sample of 101 women with metastatic or recurrent breast cancer.

Studies specifically on CRC are scarce and their results are controversial. Schofield et al. (2016) found that depression was associated with CRC survival in a sample of patients with advanced stage CRC.[18] Lloyd et al. (2019)[19] found an association between mental illness and CRC mortality. However, although Lloyd et al. suggest this relationship, the results may be limited as it is a retrospective study. Due to the peculiarities of CRC treatment, the results must not be extrapolated to other types of cancers. Furthermore, there are no validated predictive models for medium- and long-term follow-up on these outcomes.[18–20]

Since 2010, the REDISSEC-CARESS/CCR group[21] has been conducting a study in Spain to determine risk factors for death and tumour recurrence among a cohort of patients after surgical intervention for CRC. The main aim of this prospective cohort study is to evaluate the possible association between survival and depressive symptoms detected immediately after diagnosis and prior to surgery specifically among patients with CRC.

2 | METHODS/DESIGN

2.1 | Study design and participants

This work is a prospective, observational, multicentre cohort study with a 5-year follow-up period conducted on patients after the diagnosis of CRC and prior to surgical intervention. The study population was recruited between 2010 and 2012 at 22 hospitals in the Spanish National Health System. It included patients diagnosed with stage I–IV CRC who were scheduled to undergo surgery for the first time. A total of 3915 patients were initially recruited. All patients who completed the 5-year follow-up period and underwent screening for depressive symptoms at the time of diagnosis were considered for inclusion. In total, 2602 patients (65.77%) met these criteria and were included. Participants who were not evaluated in the

analysis were excluded, mainly due to their refusal to participate or because they were found not to have CRC. No statistically significant differences in terms of sex or age were found between patients included and those who refused to participate. This information can be found in Figure 1.

The inclusion criteria were the following: (1) diagnosis of cancer of the colon (CC) (up to 15 cm above the anal margin) and/or rectum (CR) (between the anal margin and 15 cm above it) who underwent curative and/or palliative surgery for the first time; (2) pathological diagnosis of CC or CR after a colonoscopy and biopsy; (3) signing of an informed consent form. The exclusion criteria were: (1) CC or CR in situ; (2) severe mental or physical disability that impeded completion of the questionnaires.

2.2 | Procedure

After patients were recruited and signed an informed consent form, data for the study was collected directly from the patients and their medical records. Data on survival at 5 years after diagnosis were obtained from hospital databases, patient/family questionnaires and Spain's National Death Index. This project was approved by the ethics committees of the participating hospitals (Approval Number: 11/23/2010). The detailed protocol for this study has been published previously.[21]

2.3 | Study variables

Symptoms of depression were measured using the Hospital Anxiety and Depression Scale (HADS-D)[22] adapted for Spain by Terol et al.[23] The HADS-D is a widely used self-administered questionnaire designed to assess depressive symptoms in hospital and psycho-oncology settings.[6,13,18,23–27] It consists of 14 items scored on a Likert scale ranging from 0 to 3 and it has good sensitivity and specificity.[22,28,29] The total score is obtained by adding scores on the 14 items and is interpreted as follows: 0–7: no depression; 8–10: probable depression; 11–21: positive depression. In this study, a HADS-D score >8 points was used as the cut-off point for depressive symptoms, in accordance with the criteria used in other studies.[6,18,24,26–28,30]

The following information was gathered from the patients' medical records: sex, age, body mass index (BMI), smoking, family history of cancer or CRC, date of first contact with the hospital, diagnosis and start of treatment, existence of previous CRC screening, tumour location (rectum/colon), histological type (conventional, mucinous or other adenocarcinoma), degree of histological differentiation, stage, lymphovascular or perineural invasion and metastasis. Data on survival was obtained at 5 years of follow-up.

2.4 | Statistical analysis

The descriptive analysis performed included measures of central tendency and dispersion for quantitative variables and frequency distributions for qualitative variables. A bivariate analysis was performed to assess differences among patients grouped according to HADS-D score categories (including the probable category). Student's *t* test was used for quantitative variables and the chi-square test for qualitative variables. Subsequently, a survival analysis was performed using the Kaplan–Meier estimator with patients grouped according to the presence (including probable cases) or absence of depressive symptoms and stratified according to the presence of metastases. Differences were evaluated using the logrank test. Finally, crude and multivariate Cox regression

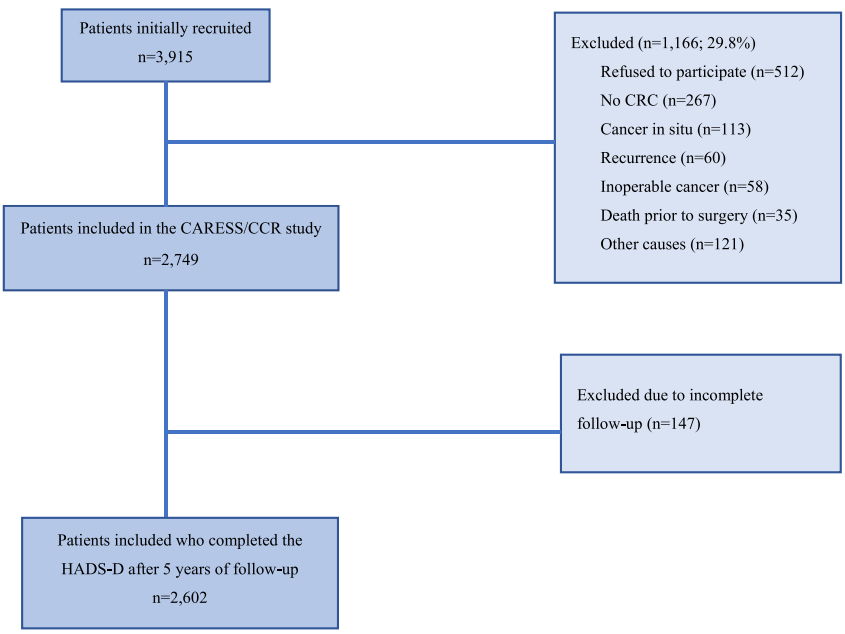

FIGURE 1 Flow chart of selection and follow-up

models were calculated with overall survival as the dependent variable and using a backward and forward stepwise strategy to select the most parsimonious model. The resulting hazard ratios were then described with their respective 95% confidence intervals. The multivariate Cox model initially included variables found to be significant in the crude analysis and those with less than 20% losses. For all analyses, the level of statistical significance was defined as $p < 0.05$. The data analysis was performed using SPSS software version 28.0.

3 | RESULTS

3.1 | Characteristics of the participants

A total of 2602 patients completed the 5-year follow-up period and the HADS-D questionnaire. Of them, 1662 (63.9%) were male. The mean age of the participants was 68 years (SD = 10.9), 1818 (72.5%) were married or in a relationship and 1928 (76.6%) had a primary school education or less. Among the patients with CRC, 1288 (54.2%) needed help from another person, but 2011 (83.3%) did not receive any type of social assistance. Regarding cancer characteristics, 191 (12.7%) patients had a family history of CRC, 181 (10%) had metastasis and 429 (18.8%) had been diagnosed following a screening test. The remaining sociodemographic and clinical characteristics are shown in Table 1.

3.2 | Profile of patients with CRC and depression

Our analysis revealed a baseline prevalence of depressive symptoms of 23.8% (619). Among the clinical and sociodemographic characteristics of the patients with depression and CRC, the following profile was observed (see Table 2): there was a higher prevalence of depressive symptoms among women than men ($p < 0.001$) and among patients ≥70 years ($p < 0.001$). There was a significantly greater prevalence ($p < 0.001$) of depressive symptoms among widowed or separated/divorced patients than among those who were married, in a relationship or single. Patients with a medium-low level of education presented with more depressive symptoms than those with a medium-high level of education ($p = 0.001$).

Regarding their social situation, patients who needed some kind of help ($p = 0.001$), received social assistance ($p < 0.001$) or lived alone ($p = 0.011$) had a higher incidence of depressive symptoms than those who did not need help or receive any type of social assistance or those who lived with relatives or in a care home.

No significant association was detected between symptoms of depression and BMI. Non-smokers were more likely to have depressive symptoms than smokers or ex-smokers ($p = 0.004$).

Finally, with regard to CRC characteristics, no significant differences were noted in terms of family history of CRC, tumour size, nodule staging, degree of tumour differentiation or histological diagnosis (see Table 2). However, statistically significant differences were found regarding the location of the tumour ($p = 0.008$), with

TABLE 1 Sociodemographic and clinical characteristics of the total sample

Characteristics	Total ($n = 2602$)	%[a]
HADS-depression		
Normal (<8)	1983	76
Probable case (8–11)	291	11
Positive case (>11)	328	13
Sex		
Male	1662	64
Female	940	36
Age[1] (Mean—SD)	68.0	10.9
Marital status[2]		
Single	188	8
Married-relationship	1818	72
Separated-divorced	117	5
Widowed	385	15
Education level[3]		
Primary school or less	1928	77
Secondary school-University	586	23
Needs help[4]		
No	1090	46
Yes	1288	54
Receives some type of social assistance[5]		
No	2011	83
Yes	403	17
Current living situation[6]		
Lives alone	338	13
Lives with family	2096	84
Lives in a care home/other	67	3
BMI[7] (Mean—SD)	27.3	7.5
Smoker[8]		
Never smoked	1105	48
Current smoker	303	13
Ex-smoker	879	39
Family history of CRC[9]		
No	1306	87
Yes	191	13
Tumour location[10]		
Right colon	661	29
Left colon	1016	44
Rectum	637	27
Tumour size[11]		
Limited local extension (T0–T1–T2)	688	30
Greater local extension (T3–T4)	1598	70

(Continues)

TABLE 1 (Continued)

Characteristics	Total (n = 2602)	%[a]
Nodule stratification[12]		
N0	1415	62
N1–N2	864	38
Degree of differentiation[13]		
Low degree	1692	87
High degree	252	13
Histological diagnosis[14]		
Adenocarcinoma	2053	91
Mucinous or other adenocarcinoma	193	9
Metastasis[15]		
Absence	1629	90
Presence	181	10
Diagnosed via screening test[16]		
Absence	1851	81
Presence	429	19

[a]Percentage by columns; Losses: 1 = 17; 2 = 94; 3 = 88; 4 = 224; 5 = 188; 6 = 101; 7 = 780; 8 = 315; 9 = 1105; 10 = 288; 11 = 316; 12 = 321; 13 = 658; 14 = 356; 15 = 792; 16 = 322.

symptoms of depression being more prevalent when the tumour was located in the right colon or the rectum rather than the left colon. Moreover, significant differences were found in terms of the absence/presence of metastasis ($p = 0.015$) and according to whether the diagnosis followed a screening test ($p = 0.005$): depression was more prevalent among patients with metastasis and those who had not been diagnosed by a screening test.

3.3 | Depression and survival

Before performing the multivariable Cox regression analysis, the relationship between depressive symptoms and survival stratified according to the presence of metastasis at tumour diagnosis was evaluated, given that the latter variable had a significant number of missing values (792 of the 2602 patients evaluated) and was excluded from the multivariable analysis.

For the total sample, mean survival was 50.4 (95% CI: 49.7–51.2) months. On the Kaplan–Meier survival analysis, when the sample was stratified for the presence of metastasis, depressive symptoms were significantly associated with poorer survival ($p < 0.001$). Among those without metastasis, patients with depressive symptoms had a lower mean survival (4.9 months) than those without them. The difference in survival attributable to the presence of metastasis was 9.7 months (Figure 2).

A crude Cox regression model was calculated to determine whether there were significant differences in survival according to depression (positive: HR = 1.77; 95% CI: 1.49–2.09) and sociodemographic variables such as sex (female: HR = 0.81; 95% CI: 0.68–0.96), age (>70 years: HR = 3.24; 95% CI: 1.90–5.52), marital status (widowed: HR = 1.48; 95% CI: 1.05–2.1), education (secondary-university: HR = 0.75; 95% CI: 0.62–0.92), need for help (HR = 1.75; 95% CI: 1.48–2.08) and provision of social assistance (HR = 1.85; 95% CI: 1.53–2.23; Table 3).

Another crude analysis detected differences corresponding to tumour characteristics and size (T3–T4: HR = 2.26; 95% CI: 1.82–2.8), nodule staging (N1–N2: HR = 2.54; 95% CI: 2.16–3.0), tumour differentiation (high grade: HR = 2.26; 95% CI: 1.82–2.8), metastasis (HR = 4.6; 95% CI: 3.73–5.67) and diagnosis following a screening test (HR = 0.57; 95% CI: 0.44–0.72).

In the adjusted Cox model, the relationship between survival and the presence of depressive symptoms persisted (HR = 1.47; 95% CI: 1.21–1.8). In the multivariable model, an association was also observed between survival and sex (female: HR = 0.63; 95% CI: 0.51–0.76), age (>70 years: HR = 3.78; 95% CI: 1.94–7.36), need for help (HR = 1.43; 95% CI: 1.17–1.74), provision of social assistance (HR = 1.46; 95% CI: 1.16–1.82), tumour size (T3–T4: HR = 1.56; 95% CI: 1.22–1.99), nodule staging (N1–N2: HR = 2.46; 95% CI: 2.04–2.96) and diagnosis following a screening test (HR = 0.71; 95% CI: 0.55–0.91).

4 | DISCUSSION

This study analysed the association between depressive symptoms and survival among patients with CRC at 5 years after diagnosis. It was found that more than 20% of the sample had symptoms of depression at the time of their cancer diagnosis. These results confirm the high prevalence of depression among patients with CRC and are similar to findings reported in previous studies.[5,31,32]

The presence of depressive symptoms was identified as a risk factor associated with survival independently of sociodemographic and tumour characteristics, indicating that presence of these symptoms alone increases risk by nearly 50%. To the best of our knowledge, this is the first reported evidence that symptoms of depression in and of themselves can be a risk factor for mortality regardless of other clinical or pathological factors. Scientific evidence on this relationship in patients with CRC is scarce. Richardson et al. (1990)[20] evaluated depression in patients with rectal cancer following surgery and did not find an association between depression and survival, but the study analysed just 47 patients. On the other hand, Schofield et al. (2016)[18] studied 429 patients with metastatic CRC for a mean of 31 months and found that depression was associated with survival in patients with advanced-stage disease.[18] Lloyd et al. (2019)[19] analysed the association between mental illness and mortality at 5 years after a diagnosis of CRC using data obtained from a medical database. The results obtained suggest that CRC survivors are at greater risk of depression than the general population at 5 years. Furthermore, after adjusting for other risk

TABLE 2 Sociodemographic and clinical characteristics of patients with CRC according to HADS-depression results

	HADS-D normal		HADS-D positive		
	n	%[a]	n	%[a]	*p*
Sex					
Male	1326	80	336	20	< **0.001**
Female	657	70	283	30	
Age					
Mean—SD	67.5	10.8	69.7	11.0	**<0.001**
Marital status					
Single	146	77	42	22	**<0.001**
Married-relationship	1429	79	389	21	
Separated-divorced	86	73	31	27	
Widowed	255	66	130	34	
Education level					
Primary school or less	1444	75	484	25	**0.001**
Secondary school-University	479	82	107	18	
Needs help					
No	952	87	138	13	**0.001**
Yes	871	68	417	32	
Receives some type of social assistance					
No	1628	81	383	19	< **0.001**
Yes	225	56	178	44	
Current living situation					
Lives alone	237	70	101	30	**0.011**
Lives with family	1625	77	471	23	
Lives in a care home/other	50	75	17	25	
BMI					
Mean—SD	27.1	7.4	27.8	80.1	0.108
Smoker					
Never smoked	808	73	297	27	**0.004**
Current smoker	234	77	69	23	
Ex-smoker	698	79	181	21	
Family history of colorectal cancer					
No	977	75	329	25	0.305
Yes	150	79	41	21	
Tumour location					
Right colon	782	73	179	27	**0.008**
Left colon	805	79	211	21	
Rectum	478	75	159	25	
Tumour size					
Limited local extension (T0−−T1–T2)	545	79	143	21	0.059
Greater local extension (T3–T4)	1206	75	392	25	

(Continues)

TABLE 2 (Continued)

	HADS-D normal		HADS-D positive		
	n	%[a]	n	%[a]	*p*
Nodule stratification					
N0	1102	78	313	22	0.112
N1–N2	647	75	217	25	
Degree of differentiation					
Low degree	1302	77	390	23	0.088
High degree	181	72	71	28	
Histological diagnosis					
Adenocarcinoma	1581	77	472	23	0.102
Mucinous or other adenocarcinoma	138	71	55	29	
Metastasis					
Absence	1261	77	368	23	**0.015**
Presence	125	69	56	31	
Diagnosed via screening test					
Absence	1383	75	468	25	**0.005**
Presence	349	81	80	19	

Note: The bold values are statistical significance $p \leq 0.05$.

Abbreviations: CRC, diagnosis of colorectal cancer; HADS-D, Hospital Anxiety and Depression Scale.

[a]Percentage by rows.

factors, there was a higher risk of death among patients diagnosed with depression.[19] The results of these studies must be interpreted with caution for several reasons. First, the study by Schofield et al. (2016)[18] was conducted on a sample of patients exclusively with metastases and in advanced stages. Second, the study conducted by Lloyd et al. (2019)[19] was a retrospective work and the diagnosis of depression was made based on data gathered from a medical database, not a direct assessment of the patients. In addition, important factors regarding clinical characteristics specific to CRC that could have influenced patient survival were not taken into account in either of these studies, such as the degree of differentiation, the histological diagnosis, lymphovascular or perineural infiltration, and whether prior CRC screening had occurred; these factors were considered in our study. Therefore, the novelty of our work's results is that it was conducted following rigorous methods on a large sample of patients and that the results obtained indicate a clear association between symptoms of depression and short survival time regardless of other risk factors.

On the other hand, this study highlights a specific profile of a patient who may be more vulnerable to depression, namely patients who are female; elderly; separated, divorced or widowed; those who have a medium-low educational level; those who live alone; those who need help or social assistance; non-smokers; those with a tumour in the right colon or rectum; those with metastasis and those who were not diagnosed by a screening test. Our findings are in line with those reported in the literature[33] except for in regard to sex. However, again, the literature on this patient population is limited. Therefore, more studies that focus on the vulnerability of patients with CRC and depressive symptoms following diagnosis are needed. This need is of particular importance given that each disease has its own characteristics.

The high incidence of depressive symptoms among patients with CRC found in this study may be explained by various factors. On the one hand, the impact of the diagnosis and uncertainty about one's future health are themselves stressful situations for these patients. In addition, the diagnostic and follow-up tests are very invasive. A colectomy,[34] use of a colostomy[35–37] and the complications that may arise as a result thereof, such as bowel obstruction, are risk factors for stress that could give rise to depressive symptoms. On the other hand, the profile of vulnerability to depression, such as the one reported in our study and in previous research,[33] may be a risk factor for depression. However, no explanatory models for these factors have been proposed.

Lastly, the results of this work lead us to question the mechanisms by which depression could affect the survival rate. Again, the literature on this issue is limited and there are no causal explanatory models specific to CRC. Previous studies conducted in patients with other types of cancer suggest that depression may interfere with treatment compliance, seeking medical care and the use of healthcare resources.[5,8,38] Associated biological factors such as endocrine deregulation[39] and inflammatory markers have also been reported.[40]

Studies conducted in patients with other types of cancers report that a reduction in depressive symptoms is associated with later survival.[11,17,41] Thus, it can be asserted that cancer's impact does not

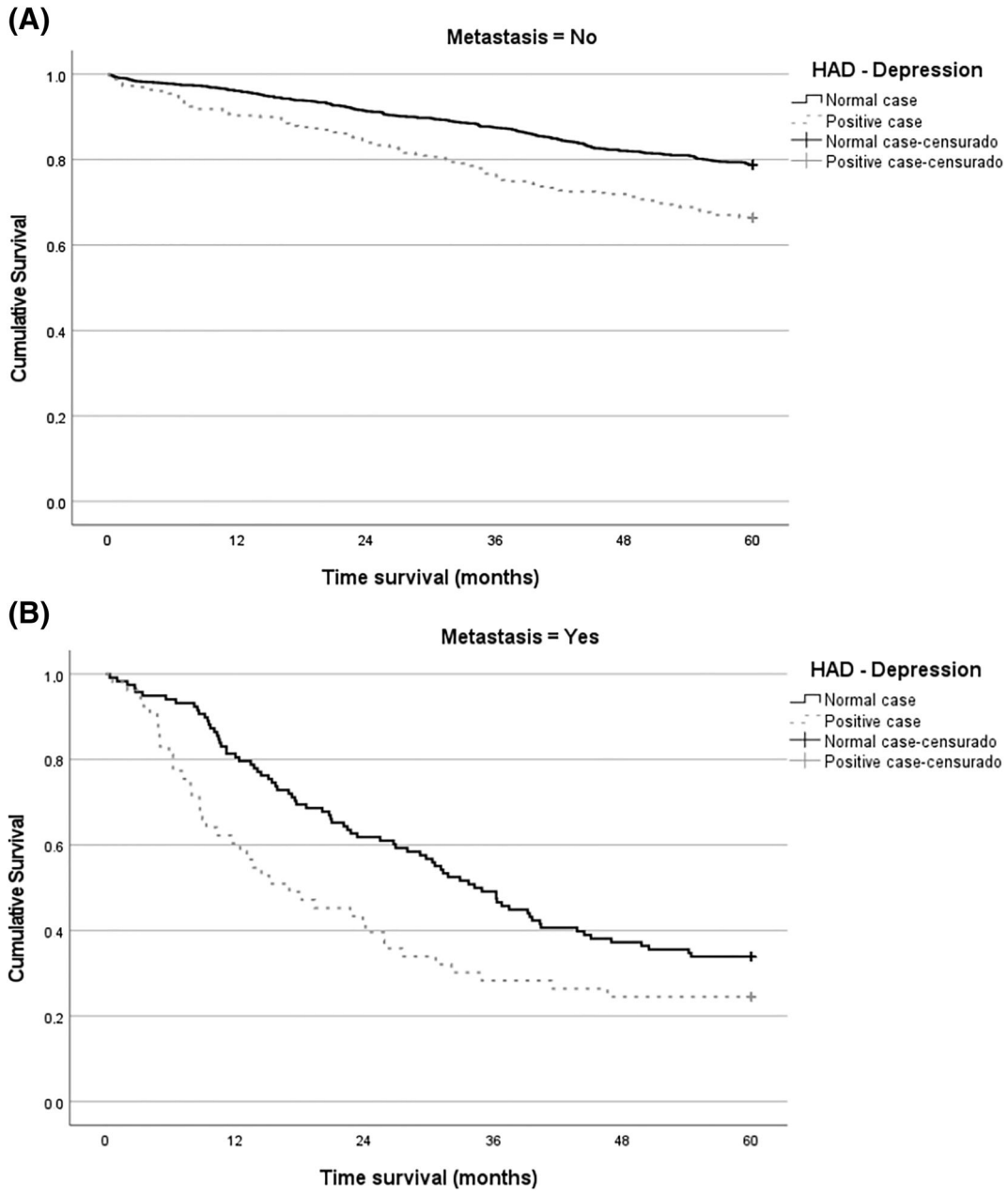

FIGURE 2 Survival curves according to presence of depressive symptoms and the absence (A) or presence (B) of metastasis

end once treatment and routine hospital follow-up are completed. Therefore, knowing each factor as well as explanatory models developed specifically for patients with CRC are fundamental for targeting early interventions for depressive symptoms.

4.1 | Clinical implications

One of this study's strengths is that it is based on a prospective study conducted in a large sample of patients from different geographical areas within the Spanish health system. It also has a 5-year follow-up period after the diagnosis of CRC and prior to surgery, providing evidence on the specific characteristics of patients with depressive symptoms and on the independent influence of these characteristics on survival. The results suggest the need to conduct psychological interventions starting at the time CRC is diagnosed, a consideration which should be taken into account in future works. Future studies should analyse whether the early detection and treatment of depressive symptoms improves survival rates. What's more, it would be interesting to know if this outcome is able to be independently reproduced regardless of whether the healthcare setting is public or private.

This study confirms the association between depressive symptoms and survival rates in CRC, as reflected in literature on other types of cancers. However, there are no works which analyse the causal mechanisms that may explain how depressive symptoms

TABLE 3 Crude and adjusted overall survival analysis using the Cox model

		Crude		Adjusted[a]	
	Mean survival (months) 95% CI	*p*	HR 95% CI	*p*	HR 95% CI
Overall	50.4 (49.7–51.2)				
HADS-depression					
Normal case	51.8 (51.1–52.7)	< **0.001**	1.00	**0.002**	1.00
Positive case	45.7 (43.9–47.5)		1.77 (1.49–2.09)		1.47 (1.21–1.80)
Sex					
Male	49.9 (48.9–50.8)	**0.013**	1.00	< **0.001**	1.00
Female	51.3 (50.1–52.5)		0.81 (0.68–0.96)		0.63 (0.51–0.76)
Age (years)					
<50	55.3 (52.7–57.9)	< **0.001**	1.00	< **0.001**	1.00
50–70	52.5 (51.5–53.4)		1.84 (1.07–3.15)		2.26 (1.16–4.40)
>70	47.6 (49.7–51.1)		3.24 (1.90–5.52)		3.78 (1.94–7.36)
Marital status					
Single	50.2 (47.4–53.0)	< **0.001**	1.00		
Married/Relationship	51.1 (50.2–51.9)		0.98 (0.71–1.34)		
Separated/Divorced	53.1 (50.1–56.2)		0.68 (0.40–1.17)		
Widowed	46.4 (44.2–48.6)		1.48 (1.05–2.10)		
Education					
Primary school or less	49.8 (48.9–50.7)	**0.006**	1.00		
Secondary/University	52.3 (50.9–53.7)		0.75 (0.62–0.92)		
Need help					
No	53.4 (52.4–54.3)	< **0.001**	1.00	< **0.001**	1.00
Yes	48.0 (46.8–49.1)		1.75 (1.48–2.08)		1.43 (1.17–1.74)
Receives social assistance					
No	51.6 (50.8–52.4)	< **0.001**	1.00	**0.001**	1.00
Yes	45.7 (43.5–47.8)		1.85 (1.53–2.23)		1.46 (1.16–1.82)
Living situation					
Lives alone	48.8 (46.6–50.9)	**0.003**	1.00		
Lives with family	50.9 (50.1–51.7)		0.82 (0.66–1.03)		
Lives in a care home/other	43.7 (37.9–49.5)		1.54 (0.98–2.41)		
Tumour size					
Limited local extension (T0–T1-T2)	55.3 (54.2–56.3)	< **0.001**	1.00	< **0.001**	1.00
Greater local extension (T3–T4)	48.8 (47.8–49.7)		2.26 (1.82–2.80)		1.56 (1.22–1.99)
Nodule staging					
N0	54.3 (53.5–55.0)	< **0.001**	1.0	< **0.001**	1.00
N1–N2	45.4 (44.0–46.8)		2.54 (2.16–3.00)		2.46 (2.04–2.96)
Tumour differentiation					
Low grade	51.2 (50.3–52.0)	**0.008**	1.00		
High grade	47.8 (45.4–50.2)		2.26 (1.82–2.80)		

TABLE 3 (Continued)

		Crude		Adjusted[a]	
	Mean survival (months) 95% CI	*p*	HR 95% CI	*p*	HR 95% CI
Metastasis					
No	52.5 (51.7–53.3)	< **0.001**	1.00		
Yes	32.5 (29.3–35.8)		4.60 (3.73–5.67)		
Screening test diagnosis					
No	49.6 (48.7–50.4)	< **0.001**	1	**0.008**	1.00
Yes	53.9 (49.6–51.1)		0.57 (0.44–0.72)		0.71 (0.55–0.91)

Note: The bold values are statistical significance $p \leq 0.05$.

[a]Cox multivariate model. Sample: 1801 patients. Only variables with statistically significant results are shown (BMI, smoking habit, family history of CRC, tumour location and histological diagnosis were not significant).

influence survival in this population of patients. Future lines of research should address this issue in order to increase the available scientific evidence.

4.2 | Study limitations

This work was designed with the aim of identifying predictive factors for depression at the time of a CRC diagnosis, which could provide guidance on future actions for treating depression and increasing survival. However, this research did not analyse the progression of depression during the follow-up period or its influence on the course of the disease. In addition, whether patients received treatment for depression after the CRC diagnosis was not examined. In light of the foregoing, it is recommended that future studies analyse the progression of depressive symptoms among CRC survivors, given that the impact of this disease does not end once treatment and follow-up are complete. Indeed, patients may continue to live with uncertainty regarding possible physical and mental health problems. Furthermore, the evaluation of some lifestyle-related factors such as alcohol use disorder or diet, which may also have some explanatory value, were not considered. Lastly, this study did not aim to detect cases of clinical depression, but rather the presence of symptoms of depression; thus, future lines of research could include clinical depression as a study variable, incorporating diagnostic interviews based on DSM-5 criteria and not just psychometric instruments, in order to analyse its influence on mortality.

5 | CONCLUSIONS

The high prevalence of symptoms of depression found in patients with CRC following diagnosis and their close relationship to survival rates suggest that their early detection and treatment should be a priority objective of the healthcare system. Furthermore, future research on this topic should specifically focus on CRC so as to provide specific results related to its characteristics so as to determine treatment needs that must be implemented to treat symptoms of depression in these patients.

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CONFLICT OF INTEREST

The authors declare they have no conflict of interest regarding this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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