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Original Article

Impact of the Preoperative Anxiety and Depression Levels on Postoperative Outcomes in Stage II/III Gastric and Colorectal Cancer Patients

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ABSTRACT

Objective: It is natural to expect chronic anxiety and depressive disorders in a cancer patient. Chronic diseases are generally investigated as potential comorbidities before surgery, whereas anxiety and depressive disorders are typically overlooked. However, psychological status plays a critical role in recovery following surgery. This study aimed to assess the prevalence of preoperative anxiety and depression in colorectal cancer (CRC) and gastric cancer (GC) patients and evaluate their effects on postoperative outcomes.

Methods: This questionnaire-based observational study enrolled 101 consecutive GC and CRC patients who underwent curative surgical resection. Preoperative anxiety and depression were assessed using the Beck Anxiety Inventory and Beck Depression Inventory 24–48 h before the surgery. Demographics and other clinical and surgical characteristics of patients were also recorded. Scores 18 and above were interpreted as clinically relevant anxiety and depression.

Results: The prevalence rates of clinically significant anxiety and depression were 16.8% and 12.9%, respectively. A significant association was found between preoperative depression and postoperative complications (p=0.006). A positive and significant correlation was found between preoperative depression and tumor stage (r=0.224, p=0.024) and neoadjuvant treatment (r=0.226, p=0.023). Higher education decreased statistically preoperative anxiety (r=−0.275, p=0.005) and depression (r=−0.283, p=0.004). There was no significant relationship between preoperative anxiety and depression and postoperative overall survival and length of hospital stay (p>0.05).

Conclusion: Our study showed that CRC patients were more exposed to both anxiety and depression in contrast to GC patients. According to our results, neoadjuvant therapy, tumor stage, and education level affected psychological distress before surgery. Identification of patients at risk of preoperative anxiety and depression using a questionnaire is reliable. A series of education of patients and their families and providing professional psychological support to those in need may improve postoperative outcomes.

INTRODUCTION

Colorectal cancer (CRC) is the third and gastric cancer (GC) is the fifth most frequently diagnosed cancer worldwide. They ranked second and third, respectively, in cancer-related mortalities.[1] Survival rates are still not at the desired level. This condition is also reflected in the mood disorders of cancer patients. It can cause psychological distress, such as anxiety and depression.[2] The prevalence of psychological distress in cancer patients may vary by the tumor type and stage, as well as the patient's age and gender. The prevalence study by Linden et al.,[3] which included 10,153 consecutive cancer patients, reported the clinic anxiety rate to be 19.0% and the depression rate to be 12.9%.

Diabetes mellitus, chronic renal and lung disease, and coronary disease are generally investigated as potential comorbidities before surgery, whereas anxiety and depressive disorders are typically overlooked and are not investigated. Psychological status, however, plays an essential role

in recovery following surgery, having been associated with poor survival outcomes,[4] wound-related complications, and prolonged hospital stays.[5] The preoperative optimization of comorbidities is a recognized course of action promoting good postoperative results. This condition has led to introducing the term "the trimodal prehabilitation" into the medical lexicon, referring to psychological, nutritional, and exercise interventions.[6] Preoperative education has also been demonstrated to contribute to reducing preoperative anxiety and depression.[7]

Preoperative anxiety and depression have been well investigated regarding their effects on the outcome among cardiac patients.[8] However, there is limited research in GC and CRC cancer patients. We aimed to investigate the prevalence of preoperative anxiety and depression in patients with gastric and CRC and evaluate their effects on postoperative results.

MATERIALS AND METHODS

This questionnaire-based observational study screened 101 consecutive gastric and CRC patients who underwent curative surgical resection in our hospital between January 2018 and September 2019. The institutional review board of Koşuyolu Higher Specialty Training and Research hospital approved the study protocol, which was in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each participant, and the ethics committee of Koşuyolu Higher Specialty Training and Research hospital granted ethical approval (No.: 2019/3/97).

The study included patients aged ≥18 years, who were conscious and cooperative, who provided their informed consent, and who were scheduled for elective curative surgery under the diagnosis of nonmetastatic GC and CRC. The study excluded patients who had a diagnosis of current or an altered psychiatric disorder, who were taking antidepressants, anxiolytics, or antipsychotics, and who had palliative surgery.

Preoperative anxiety and depression were assessed using the Beck Anxiety Inventory (BAI)[9] and the Beck Depression Inventory (BDI)[10] 24–48 h before the surgery. Demographics and other clinical and surgical characteristics of patients were also recorded.

Turkish translation and validation studies of BAI and BDI were conducted by Ulusoy et al.[11] and Hisli,[12] respectively. Both inventories consist of 21 statements, the assessment is performed on a scale ranging from 0 to 3 according to the responses reported for each category, and the higher possible score was 63. According to these scores, the levels of anxiety are classified as mild (0–17), moderate (18–24), and severe (25–63), and the levels of depression as no depression (0–10), mild (11–17), moderate (18–23), and severe (24–63). The cut-off values were found to be 17 in both studies, with scores of 18 and above interpreted as anxiety and depression. The classification of the surgical complications that were considered in the first 30 days was based on the Clavien–Dindo grading.[13]

Statistical analysis

The SPSS (Statistical Product and Service Solutions) software version 22 for Windows (Statistical Package for the Social Sciences) was used for statistical analyses of the study. The normality of the distribution of the data was carried out using the Kolmogorov–Smirnov test. Qualitative data were presented as frequency and percentage. Quantitative data were given as mean±SD if the data were normally distributed, and median (interquartile range) if the data were not normally distributed. The Mann–Whitney U test was used to examine whether anxiety and depression were related to the length of hospital stay. The association of anxiety and depression with categorical variables was analyzed using Chi-squared and Fisher's exact tests. Kaplan–Meier analysis evaluated the relationship between overall survival and anxiety and depression. Spearman's correlation test was used to analyze measurable data with one another. A p-value less than 0.05 was accepted as statistically significant.

RESULTS

Table 1 summarizes the relationship between anxiety and depression, as well as the frequency distribution of variables. This study included a total of 101 patients of whom 36 (35.6%) were females. The median age was 60 (52–70) years for anxiety and 52 (51–64) years for depression. The median follow-up time was 17.7 (15.0–18.8) months in the anxiety group and 17.7 (14.8–18.9) months in the depression group. Clinically relevant anxiety was identified in 17 patients (16.8%) and depression in 13 patients (12.9%). A statistically significant prolongation of hospital stay was not observed in both groups. The percentage of high school education in the study population was 31.7%. Approximately, two-thirds of the patients in the study were CRC patients. Both anxiety and depression were higher in CRC patients. The cancer location was not significantly associated with anxiety and depression ($p>0.05$). The number of patients with stage III was higher than stage II (56.4% vs 43.6%). The proportion of those who received neoadjuvant treatment was 29.7%. There was no significant relationship between preoperative anxiety and depression of gender ($p=0.974$ vs $p=0.767$, respectively). However, a significant association was found between preoperative depression and surgical complications ($p=0.006$). The impact of preoperative anxiety and depression on the length of hospital stay was not observed ($p=0.124$ vs $p=0.497$, respectively).

Higher education was found to statistically decrease preoperative anxiety ($p=0.005$) and depression ($p=0.004$), indicating a mild negative correlation ($r=-0.275$ vs $r=-0.283$, respectively). The depression increased significantly with tumor progression ($p=0.024$). Similarly, neoadjuvant treatment was positively correlated with preoperative depression ($r=0.226$, $p=0.023$) (Table 2).

In addition, neither preoperative anxiety nor depression

Table 1. Patient's demographic, clinical, and surgical characteristics

Variables		Total (n=101)	Anxiety, BAI ≥18 (n=17)		Depression, BDI ≥18 (n=13)	
		n (%)	n (%)	p	n (%)	p
Age (years)	<65	71 (70.3)	11 (64.7)	0.580[a]	10 (76.9)	0.750[b]
	≥65	30 (29.7)	6 (35.3)		3 (23.1)	
Sex	Male	65 (64.4)	11 (64.7)	0.974[a]	9 (69.2)	0.767[b]
	Female	36 (35.6)	6 (35.3)		4 (30.8)	
Active smoker	Yes	11 (10.9)	1 (5.9)	0.685[b]	2 (15.4)	0.631[b]
	No	90 (89.1)	16 (94.1)		11 (84.6)	
Alcohol	Yes	2 (2)	0 (0.0)	>0.999[b]	0 (0.0)	>0.999[b]
	No	99 (98)	17 (100.0)		13 100.0)	
≥ High school education	Yes	32 (31.7)	3 (17.6)	0.173[a]	2 (15.4)	0.217[b]
	No	69 (68.3)	14 (82.4)		11 (84.6)	
AJCC TNM stage	II	44 (43.6)	5 (29.4)	0.197[a]	3 (23.1)	0.110[a]
	III	57 (56.4)	12 (70.6)		10 (76.9)	
Tumour location						
	Gastric	35 (34.7)	4 (23.5)	0.291[a]	5 (38.5)	0.763[b]
	Colorectal	66 (65.3)	13 (76.5)		8 (61.5)	
Comorbidity	Yes	43 (42.6)	7 (41.2)	0.898[a]	6 (46.2)	0.780[a]
	No	58 (57.4)	10 (58.8)		7 (53.8)	
BMI (kg/m^2)	<30	70 (69.3)	12 (70.6)	0.900[a]	7 (53.8)	0.211[b]
	≥30	31 (30.7)	5 (29.4)		6 (46.2)	
Neoadjuvant therapy	Yes	30 (29.7)	6 (35.3)	0.580[a]	7 (53.8)	0.054[b]
	No	71 (70.3)	11 (64.7)		6 (46.2)	
ASA	<3	45 (44.6)	7 (41.2)	0.759[a]	7 (53.8)	0.470[a]
	≥3	56 (55.4)	10 (58.8)		6 (46.2)	
Complication	Yes	58 (57.4)	13 (76.5)	0.082[a]	12 (92.3)	0.006[a]
	No	43 (42.6)	4 (23.5)		1 (7.7)	
			Median (IQR)		**Median (IQR)**	
Length of stay/day			10 (8–17)	0.124[c]	9 (8–12)	0.497[c]

[a]Chi-square test; [b]Fisher's exact test; [c]Mann-Whitney U test; AJCC: American Joint Committee on Cancer; TNM: Tumor/Node/Metastasis; ASA: American Society of Anesthesiologists; BMI: Body Mass Index.

had any association with overall survival (p=0.867 vs p=0.125, respectively) (Table 3 and Fig. 1).

DISCUSSION

This observational study used BAI and BDI to measure the prevalence of preoperative psychological distress such as anxiety and depression level and its impact on postoperative outcomes among stage II/III GC and CRC patients undergoing elective, curative surgery. Our results suggested some risk factors that influence psychological distress in the preoperative phase, such as neoadjuvant therapy, tumor stage, and education level.

Recent studies have started to include anxiety and depressive disorders in the preoperative evaluation of patients. Preoperative psychological distress leads to the activation

of sympathetic and parasympathetic nervous systems, increased blood pressure due to catecholamine secretion, bronchial dilatation, tachycardia, tachypnea, and decreased gastrointestinal system functions and secretions.[14] The successful effects of physiological preparation on postoperative results in cancer patients scheduled for surgery are well known. Similarly, psychological preparation is equally important.[6,15]

Table 2. Correlation analysis of the factors affecting anxiety and depression

Variables	Anxiety		Depression	
	r	p	r	p
Education	-0.275	0.005	-0.283	0.004
TNM stage	0.166	0.097	0.224	0.024
Comorbidity	0.053	0.596	0.048	0.630
Neoadjuvant therapy	0.166	0.096	0.226	0.023
ASA score	0.112	0.266	0.088	0.384

ASA: American Society of Anesthesiologists; TNM: Tumor/Node/Metastasis.

Magno et al.[16] have stated that neoadjuvant therapy may induce psychological distress in breast cancer patients, and mental support may help this patient group. Our study can conclude that neoadjuvant therapy is a risk factor for preoperative depression. In addition, the relationship between education level and depression was evaluated, and similar to our results, it was reported that higher education is a potential protective factor for depression.[17] The study by Ghoneim and O'Hara,[15] which evaluated all four stages of GC in 229 patients, found the depression rate higher among those with an advanced cancer stage and with a low level of education. Likewise, stage III patients of our study were significantly more depressed than stage II patients.

The overall survival of cancer patients with psychological distress is more reduced than those without.[15] Kaplan–Meier analysis in our study did not confirm this information. It should be mentioned here that the follow-up duration in the present study was relatively short, which might have affected the results.

The present study observed statistically significant early postoperative complications in 12 of 13 patients with pre-

Table 3. Survival analysis of anxiety and depression levels

	Median (IQR)	Estimate	Std.error	95% CI (Lower and upper Bound)	p
Anxiety level	7 (4–12)				
Beck anxiety index <18		27.697	0.672	26.379–29.015	0.867
Beck anxiety index ≥18		25.487	1.486	22.575–28.400	
Depression level	8 (4–14)				
Beck depression index <18		28.018	0.609	26.825–29.212	0.125
Beck depression index ≥18		23.708	2.011	19.766–27.650	

IQR: Interquartile Range; CI: Confidence Interval.

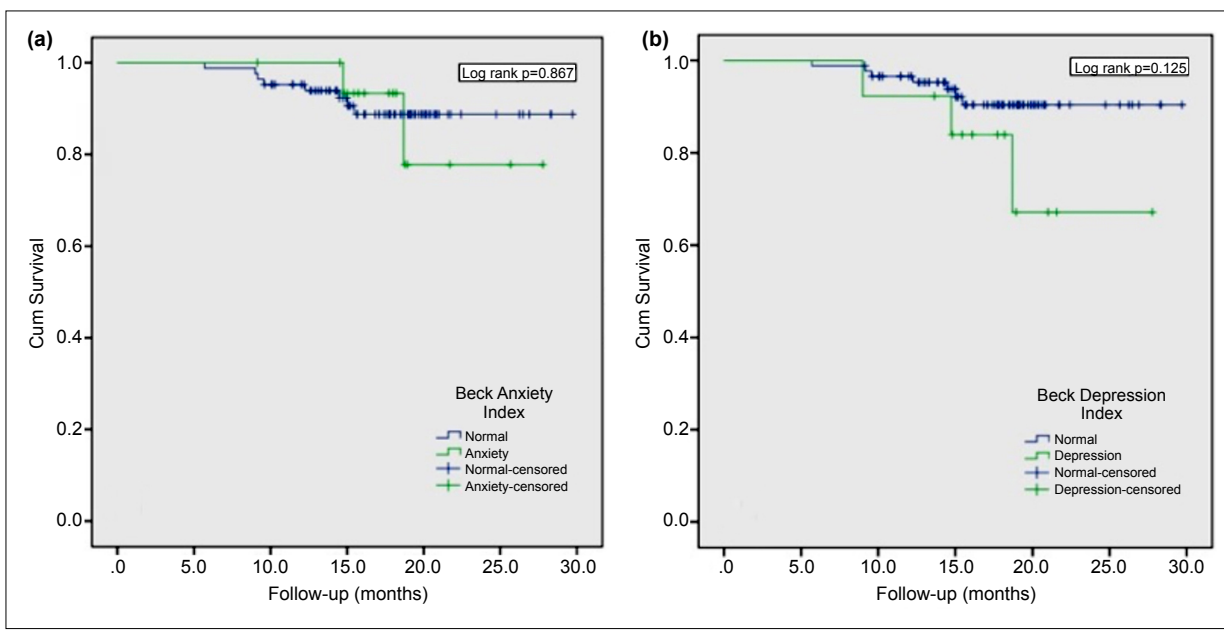

Figure 1. Association between overall survival and anxiety **(a)** and depression **(b)**.

operative depression. According to the literature, postoperative complications, especially those involving infections, may increase due to decreased immunity in cancer patients, neoadjuvant treatment, increased psychological distress such as depression, which causes noncompliance to treatment, and low preoperative functional performance (FP).[4,15] This condition is one of the main factors leading to prolonged hospital stays. Depression increased the complication rate in this study but did not affect the length of the postoperative hospital stay.

Preoperative good FP is one of the essential features for an active postoperative period. A poor FP is more frequent in depressive patients. Decreased FP is associated with a prolonged hospital stay, weak functional recovery, poor operative outcomes, and increased mortality.[4,15] Patients presenting with preoperative depressive symptoms were found to benefit more from a 4-week program of preoperative and an 8-week program of postoperative prehabilitation interventions including exercise, nutritional, and stress reduction components than traditional postoperative rehabilitation activities.[4] Küchler et al.[18] compared gastric, pancreatic, liver, and colon cancer patients who received a formal psychotherapeutic support program during their hospital stays with those who did not, and the psychotherapeutic support recipients had better survival. Prehabilitation interventions appear to be a promising solution to this problem. Psychological preparation comprises a 60–90 min conference with a psychologist and preparing in unwinding methods and breathing activities other than conveying material with practice recordings to be done at home. Cognitive preparing as psychological counseling, reflection, or yoga may likewise lessen perioperative anxiety and stress.[19] Psychological assessments using questionnaires can be used in patient selection and identify risky patients. However, there is a challenge here, as a diagnosis of psychological status based on preoperative questionnaires could be problematic ethically and may be affected by the limitations of the scoring tools.[20] In addition to prehabilitation interventions, Guo et al.[7] have reported that a preoperative education intervention comprising information leaflets and verbal advice decreased preoperative anxiety and depression of patients before cardiac surgery.

Our study had several limitations. First, anxiety and depression were not compared between the preoperative and postoperative periods. Second, the duration of the follow-up was relatively short. Third, data about economic and marital status, social support, living situation, and cancer diagnosis date were not collected. Fourth, these data were based on self-reported questionnaires. It may be over- or underestimated. Finally, although the present study limited the number of cancerous organs and cancer stages to only two, both of these different organs and stages might have affected the survival outcomes.

One of the strengths of the study is that early and metastatic stages (stage I and IV), which have a direct effect on survival, were excluded. Additionally, this study addresses a current issue that focuses on the preoperative period and may help improve postoperative outcomes in psychologically stressed cancer patients.

In conclusion, our study showed that CRC patients were more exposed to both anxiety and depression in contrast to GC patients. According to our results, neoadjuvant therapy, tumor stage, and education level affected psychological distress before surgery. The identification of patients at risk of preoperative anxiety and depression using a questionnaire is reliable. A series of education of patients and their families and providing professional psychological support to those in need may improve postoperative outcomes. Randomized and controlled trials are required to clarify this subject further.

Ethics Committee Approval

This study approved by the Kartal Koşuyolu Higher Specialty Training and Research Hospital Clinical Research Ethics Committee (Date: 26.09.2019, Decision No: 2019/3/97).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: S.G., A.S.S., S.Ö.; Design: A.D., O.U., U.D.; Supervision: S.G., A.D., E.P.; Fundings: O.U., A.S.S., M.D.; Materials: S.G., A.D.; Data: S.Ö., O.U.; Analysis: O.U., A.S.S.; Literature search: S.G., U.D., E.P.; Writing: S.G., A.D., S.Ö., M.D.; Critical revision: S.G., E.P., M.D.

Conflict of Interest

None declared.

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Evre II/III Mide ve Kolorektal Kanserli Hastalarda Ameliyat Öncesi Anksiyete ve Depresyon Düzeylerinin Ameliyat Sonrası Sonuçlara Etkisi

Amaç: Kanser hastasında kronik anksiyete ve depresyon beklenmesi doğaldır. Diğer kronik hastalıklar ameliyattan önce potansiyel komorbiditeler olarak genellikle araştırılırken, anksiyete ve depresyon tipik olarak göz ardı edilir. Ancak psikolojik durum ameliyat sonrası iyileşmede kritik rol oynar. Bu çalışma kolorektal kanser (CRC) ve mide kanseri (GC) hastalarında ameliyat öncesi anksiyete ve depresyon prevalansını belirlemeyi ve ameliyat sonrası sonuçlar üzerine etkilerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Anket tabanlı bu gözlemsel çalışmaya küratif cerrahi rezeksiyon uygulanan ardışık 101 mide ve kolorektal kanser hastası dahil edildi. Ameliyat öncesi anksiyete ve depresyon, ameliyattan 24–48 saat önce Beck Anksiyete Ölçeği (BAI) ve Beck Depresyon Ölçeği (BDI) kullanılarak değerlendirildi. Hastaların demografik özellikleri, klinik ve cerrahi verileri de kaydedildi. On sekiz ve üzeri puanlar klinik olarak anksiyete ve depresyon ilişkili yorumlandı.

Bulgular: Klinik olarak anlamlı anksiyete ve depresyon prevalans oranları sırasıyla %16.8 ve %12.9 idi. Ameliyat öncesi depresyon ile ameliyat sonrası komplikasyonlar arasında anlamlı bir ilişki saptandı (p=0.006). Ameliyat öncesi depresyon ile tümör evresi (r=0.224, p=0.024) ve neoadjuvan tedavi (r=0.226, p=0.023) arasında pozitif ve anlamlı bir ilişki olduğu görüldü. Yüksek eğitim düzeyi, istatistiksel olarak ameliyat öncesi anksiyeteyi (r=-0.275, p=0.005) ve depresyonu (r=-0.283, p=0.004) azaltığı gözlendi. Ameliyat öncesi anksiyete ve depresyon ile ameliyat sonrası genel sağkalım ve hastanede kalış süresi arasında anlamlı bir ilişki yoktu (p>0.05).

Sonuç: Çalışmamız, KRK hastalarının GC hastalarına kıyasla hem anksiyete hem de depresyona daha fazla maruz kaldığını göstermiştir. Sonuçlarımıza göre neoadjuvan tedavi, tümör evresi ve eğitim düzeyi ameliyat öncesi psikolojik distresi etkiledi. Bir anket kullanılarak ameliyat öncesi anksiyete ve depresyon riski taşıyan hastaların belirlenmesi güvenilirdir. Hastaların ve ailelerinin eğitimleri ve ihtiyaç sahiplerine profesyonel psikolojik destek sağlanması, ameliyat sonrası sonuçları iyileştirebilir.

Anahtar Sözcükler: Anksiyete; depresyon; kolorektal kanser; mide kanseri; psikolojik distres.