Original Article

A cross-sectional study of obstructive sleep apnea in patients with colorectal cancer

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Background: The association between colorectal cancer (CRC) and obstructive sleep apnoea (OSA) has been attracting increasing attention. several studies had confirmed that OSA increases the risk of CRC onset. However, the findings of studies on the morbidity of OSA in patients with CRC were unclear. Therefore, this study aimed to investigate the morbidity of OSA in patients with CRC as well as the association between the clinicopathological characteristics of OSA and CRC.

Methods: A total of 414 patients with a pathological diagnosis of CRC from 1 January, 2020 to 30 December, 2020 were included in this study. Demographic characteristics, clinical information, and tumor characteristics of participants were collected; sleep was monitored using a wearable oximeter and via sleep quality questionnaire. The oxygen desaturation index (ODI) was used to classify OSA severity so that the diagnostic criteria for OSA were set based on the ODI as 0–5 (normal) and ≥5 (abnormal). After correcting for confounding factors, a logistic regression analysis was performed to calculate the odds ratio (OR) and 95% confidence interval (CI) for the factors affecting the tumor lymph node stage (N stage).

Results: A total of 402 patients with CRC were included in this study, including 225 (55.97%) men and 177 (44.03%) women. The mean ODI value of participants was 3.40±8.17. The morbidity of OSA among the patients with CRC having ODI ≥5 was 16.17%. A comparison between the normal and abnormal ODI value groups revealed that the high proportion of abnormal ODI was related to higher N stage ($P<0.05$). Logistic regression analysis revealed a correlation of ODI values and age to the N stage. Specifically, CRC patients with an abnormal ODI had a higher risk of lymph node metastasis compared to those with normal ODI (OR =1.915, 95% CI: 1.025 to 3.579). Moreover, patients with CRC aged ≥65 years had a higher risk of lymph node metastasis compared to those aged <65 years (OR =2.190, 95% CI: 1.163 to 4.125).

Conclusions: CRC patients with abnormal ODI are susceptible to OSA. Additionally, abnormal ODI and age ≥65 years are relevant factors for the N2 stage.

Keywords: Colorectal cancer (CRC); obstructive sleep apnea (OSA); oxygen desaturation index

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Introduction

Obstructive sleep apnea (OSA) is primarily characterized by the repeated collapse of the upper airway during sleep, causing apnea and/or hypoventilation. This results in intermittent hypoxia (IH) and sleep fragmentation that can cause a complex series of pathophysiological changes (1), leading to multi-system and multi-organ damage. It is also an independent risk factor for hypertension, cardiovascular disease, cerebrovascular disease, and metabolic disease (2-5). According to the sleep apnea-hypopnea index (AHI) established by the American Academy of Sleep Medicine in 2012, approximately one billion people worldwide are affected by mild-to-moderate-to-severe OSA. With nearly 176 million (13.0%) cases, China has the highest prevalence of OSA globally (6).

Currently, the relationship between malignancy and OSA, one of the major chronic diseases, is gaining attention. OSA is associated with an increased overall incidence of malignancy (7), and a higher risk of moderate to severe OSA (8). Moreover, between 2007 and 2017, colorectal cancer (CRC) cases have increased by 38% worldwide (9). In 2020, CRC was the third leading contributor of malignancy and the second leading contributor of morbidity, with 555,000 new cases (16.8%) and 286,000 deaths (11.8%) in China (10). Studies on the relationship between OSA and CRC have confirmed that OSA can increase the risk of CRC onset. Zhang *et al.* reported on the association between sleep disorders and CRC (11) in 1,973 patients with OSA (1.9%) and obesity, snoring, and sleep duration >9 h, who were diagnosed with malignant CRC during a 22-year follow-up period. In a study in South Korea, 18 of 111 patients with OSA (16.2%) were diagnosed with advanced CRC after 15 years of follow-up, a rate approximately 3.03 times higher than that of controls (12). A study from Taiwan reported that the risk of CRC onset was significantly higher in patients with OSA than in those without (13). However, to the best of our knowledge, Current studies have focused on OSA increasing the risk of CRC, there have been no studies on the morbidity of OSA among patients with CRC, the clinicopathological features and prognosis of CRC patients with OSA have not been studied yet.

Based on the current findings of the Chinese CRC big data survey (10) and the changing dietary and lifestyle habits of Chinese residents, CRC, a highly prevalent tumor, was selected as an entry point to investigate the morbidity of OSA and sleep status of patients with CRC. Additionally, the correlation between OSA and important indicators, such as clinicopathological characteristics, was evaluated to substantiate the evidence supporting the diagnosis, treatment, and overall management of patients with CRC. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-175/rc).

Methods

Inclusion and exclusion criteria

A total of 414 patients with CRC who attended the Departments of Gastrointestinal Surgery, Anorectal Surgery, Medical Oncology, and Oncology Radiotherapy at Huizhou Municipal Central Hospital, Huizhou, Guangdong, China, between January 2020 and December 2020 were included in this study. The inclusion criteria included age ≥18 years and definite CRC pathological diagnosis. The exclusion criteria included incomplete patient information and other tumor types at the time of sleep monitoring or that had been previously reported (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Huizhou Municipal Central Hospital. All patients voluntarily participated in this study and provided informed consent.

Baseline characteristics

The following characteristics were considered as the baseline.

(I) Demographic characteristics including gender, age, height, weight, body mass index (BMI), and neck circumference.

(II) Smoking and alcohol consumption history: a smoking history was defined as smoking at least 1 cigarette per day for more than 6 months at the time of check-up, regardless of whether the smoker had quit smoking; a non-smoker was defined as having no history of smoking (14). Additionally, alcohol consumption history was defined as more than 5 years of alcohol consumption, equivalent to ≥40 g/d of alcohol or a history of binge drinking within the past 2 weeks (15).

(III) Comorbidities: Hypertension was defined as being on antihypertensive medication or having a systolic blood pressure of more than 140 mmHg

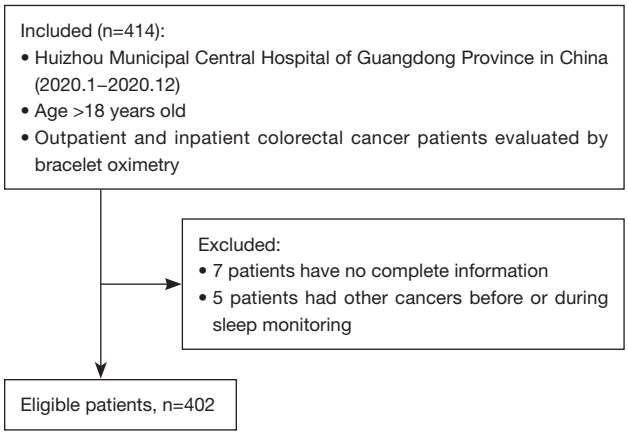

Figure 1 Inclusion and exclusion criteria.

or diastolic blood pressure of more than 90 mmHg measured on 3 consecutive occasions (more than 3 minutes apart). Diabetes mellitus was defined as random blood glucose ≥11.1 mmol/L or fasting-blood glucose (i.e., no food intake for at least 8 hours before testing) ≥7.0 mmol/L. Coronary artery disease (CAD) was defined as the condition caused by atherosclerosis of the coronary arteries resulting in luminal stenosis or occlusion, which leads to myocardial ischemia and hypoxia or necrosis, including acute coronary syndrome and chronic CAD.

(IV) Clinical and pathological characteristics: Origin sites included the colon or rectum, left hemicolon (including the descending colon, sigmoid colon, and left half of the transverse colon) and right hemicolon (including the cecum, ascending colon, and right half of the transverse colon).

Tumor-node-metastasis (TNM) staging included T1-4, N1-2, and M0-1 according to the 2018 American Joint Committee on Cancer: Colorectal Cancer (16).

Treatment modalities included surgery, chemotherapy, radiotherapy, targeted therapy, immunotherapy, and supporting therapies. Sleep was monitored before surgery and ≥2 months after surgery. Pathological types included adenocarcinoma and other types; the cell differentiation degree included poorly, moderately, and highly differentiated cells.

(V) Scale information: The Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality of patients with CRC (17). The scale indicators included sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of hypnotic drugs, and daytime dysfunction. A final total PSQI score ranging from 0 to 21 was derived, with higher scores being associated with poorer sleep quality. The scale was distributed to patients and collected on the spot during their outpatient visits or hospitalization.

OSA screening in patients with CRC

Patients with gastrointestinal tumors often suffer from abdominal pain and distension, abnormal defecation, fatigue, poor appetite, and have difficulty tolerating polysomnography (PSG) monitoring and low compliance. In this study, the Cloudcare Healthcare Wearable Oximeter (Cloudcare Healthcare, Chengdu, Sichuan, China) was used for sleep monitoring, which was a coin-sized patch with 3M medical human double-sided tape. The oximeter is simple to operate and excludes the changes influenced by the sleep environment on sleep quality. Meta-analysis also suggested that such devices could serve as a viable alternative to PSG for clinically suspected OSA (18). Moreover, it is suitable for use in specific oncology populations, especially patients with bowel cancer.

Briefly, personal information was entered in the portable oximeter system, and it was positioned onto the thenar eminence of the hand at bedtime. The palm was cleaned before the positioning, and it automatically monitored the patient's sleep status from 11:00 pm to 6:00 am. After monitoring, the portable oximeter was removed and switched off for storage and data collection.

Sleep monitoring information included total sleep time (TST), oxygen desaturation index (ODI), mean oxygen saturation ($MSaO_2$), lowest oxygen saturation ($LSaO_2$), and the percentage of night-time spent with oxygen saturation less than 90% (Tsat90).

Definition of OSA

The ODI, which indicates the number of reactive oxygen species produced during the transition from short periods of repeated hypoxia to a normal state (19), is a highly accurate predictor of AHI and mild, moderate, and severe OSA. With AHI ≥5 as a screening criterion for OSA, the accuracy of diagnosing OSA was 87% (20). Moreover, the predictive value of the ODI is higher than that of AHI in predicting OSA-related hypertension (21,22). Therefore,

Table 1 Clinical characteristics of patients with CRC

Variables	N (%)/($\bar{x}$ ± SD)
Total (n)	402
Gender	
Male	225 (55.97)
Female	177 (44.03)
Age (years)	58.91±11.64
BMI (kg/m^2)	22.22±3.35
Neck circumference (cm)	38.47±6.57
Type of CRC	
Colon cancer	223 (55.47)
Rectal cancer	179 (44.53)
Tumor stage	
Stage I	42 (10.50)
Stage II	104 (26.00)
Stage III	145 (36.25)
Stage IV	109 (27.25)
CEA (ug/L)	
Normal	250 (63.13)
Abnormal	146 (36.87)
CA19-9 (ug/L)	
Normal	294 (77.37)
Abnormal	86 (22.63)
Snoring	
Yes	92 (22.89)
No	310 (77.71)
ODI	
<5	337 (83.83)
≥5	65 (16.17)
PSQI score	8.49±4.57
TST (h)	5.41±1.28
$MSaO_2$ (%)	95.21±2.80
$LSaO_2$ (%)	80.90±8.05
Tsat90 (%)	8.44±16.33

BMI, body mass index; CEA, carcinoembryonic antigen; CA19-9, glycoprotein antigen 19-9; ODI, oxygen desaturation index; PSQI, Pittsburgh Sleep Quality Index; $MSaO_2$, mean oxygen saturation; $LSaO_2$, lowest oxygen saturation; Tsat90, the percentage of night-time spent with oxygen saturation less than 90%; TST, total sleep time; CRC, colorectal cancer.

the diagnostic criteria for OSA were set based on the ODI as 0–5 (normal) and ≥5 (abnormal).

Statistical analyses

The software SPSS 19.0 (IBM Corp., Chicago, IL, USA) was used for statistical analyses. The measurement data were expressed as mean ± standard deviation, and comparison between groups was performed by *t*-test or analysis of variance (ANOVA) such as the sleep indicators like TST/ODI/$MSaO_2$ etc. Additionally, the enumeration data were expressed as percentages (%), and the chi-square test was used for comparison between groups. Multivariate logistic regression analysis of the ODI values was performed using the N stage tumor of the patient as the dependent variable (N0+N1=0, N2=1) via the independent variable stepwise entry method. A 2-sided test was adopted, with the size of the test was set as α=0.05, and P<0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 402 patients with CRC were included in this study, including 225 (55.97%) men and 117 (44.03%) women. The mean age of the patients was 58.91±11.64 years. Among the test patients, 223 patients (55.47%) presented with colon cancer and 179 patients (44.53%) with rectal cancer. The site of the tumor origin was predominantly in the left hemicolon (325 cases, 80.85%). Adenocarcinoma was the predominant pathology, (383 cases, 95.27%), of which moderately differentiated adenocarcinoma was the most prevalent (268 cases, 68.26%). The mean ODI value of patients with CRC was 3.40±8.17; $MSaO_2$, 95.21%±2.80%; mean Tsat90, 8.44%±16.33%; mean PSQI score, 8.49±4.57; and the mean TST, 5.41±1.28 hours. A total of 65 of the 402 patients had an ODI value ≥5, and the morbidity of OSA in patients with CRC was 16.17%. The clinical characteristics of patients with CRC are shown in *Table 1*.

ODI and the clinicopathological characteristics of patients with CRC

Comparison of the general conditions of the different OSA groups of patients with CRC

A comparison of the general conditions of patients with

CRC in the normal- and abnormal-ODI groups revealed statistically significant differences between the groups in terms of TST, $MSaO_2$, $LSaO_2$, Tsat90, and PSQI scores. Specifically, TST, $MSaO_2$, $LSaO_2$, Tsat90, and PSQI scores in the normal-ODI group were lower than those in the abnormal-ODI group (P<0.05). Notably, the higher the Tsat90 value, the higher the proportion of ODI values ≥5 (P<0.05). The comparison of the general conditions between the 2 groups is shown in *Table 2*.

Comparison of the clinicopathological characteristics of patients with CRC in different OSA groups

A comparison of the clinicopathological characteristics of patients with CRC in 2 OSA groups revealed a statistically significant difference only during the N-stage. The ODI was not statistically significant to the tumor origin site, T-stage, M-stage, and pathology type. Among the patients with CRC, a higher proportion of patients with N2 stage disease (patients showing a greater extent of lymph node involvement) had abnormal ODI values compared to those with N0+N1 stage disease (P<0.05). The comparison of clinicopathological characteristics between the 2 groups is shown in *Table 3*.

Comparison among patients with CRC having different tumor stages

A comparison among patients with CRC having different tumor stages revealed a statistically significant difference (P<0.05) in the gender of patients in the T-stage. In the N-stage, statistically significant differences (P<0.05) in age and $LSaO_2$ were observed between the 2 groups, whereas in the M-stage, statistically significant differences (P<0.05) were observed in age and alcohol consumption (*Table 4*).

Analysis of factors influencing lymph node metastasis in patients with CRC

A binary logistic regression model with N-stage as the dependent variable (N0+N1=0, N2=1) and gender, age, ODI, $MSaO_2$, smoking, and alcohol consumption as the independent variables were used for analysis via the stepwise entry method of the independent variables. The results showed the association of ODI and age with the N-stage. Specifically, patients with an ODI ≥5 had a higher risk of lymph node metastasis compared to those with an ODI <5 [odds ratio (OR) =1.915, 95% confidence interval (CI): 1.025 to 3.579]. Additionally, patients ≥65 years had a higher risk of lymph node metastasis compared to those aged <65 years (OR =2.190, 95% CI: 1.163 to 4.125). The analysis of factors associated with N-stage in patients with CRC is detailed in *Table 5*.

Discussion

This study showed that the morbidity of OSA in patients with CRC was 16.17% using ODI ≥5 as the diagnostic criterion. Moreover, N-stage was associated with ODI values. This study, to the best of our knowledge, was the first cross-sectional study on the morbidity of OSA and sleep status in patients with CRC. The morbidity of CRC in China has been increasing annually, with a slight decrease in colon cancer and a more significant increase in rectal cancer. Differences in region, gender, and age have been observed in the ratio of colon cancer to rectal cancer, with a male-to-female gender ratio of 1.33 and a significant increase in morbidity after age >50 years (23). The patients included in this study had a gender ratio of 1.27 and a mean age of 58.91±11.64 years. Overall, the results were consistent with the overall CRC epidemiological data of China.

Previous study have reported that the morbidity of OSA in patients with head and neck tumors was approximately 59.78% (24). Additionally, 60.7% of patients with cutaneous malignant melanoma had OSA, with severe OSA observed in 14.3% (25). Moreover, up to 80% of patients with lung cancer had OSA, with 50% having moderate-to-severe OSA (AHI ≥15) (26). The morbidity of OSA in postoperative patients with renal clear cell carcinoma was 7% (27). The morbidity of OSA, as determined in this study, differed significantly in patients with head and neck tumor, cutaneous melanoma, renal cancer, and lung cancer, which can be attributed to the location of these specific tumors, treatment modalities, differences in the populations affected, comorbidities, and the biological characteristics of the tumors. In head and neck tumors, changes in the local structure of the airway due to treatment modalities are important factors contributing to the morbidity of OSA (24); patients with lung cancer have a high rate of smoking behavior and chronic obstructive pulmonary disease, which can influence the progression of OSA (26). According to the criterion of ODI ≥5, the morbidity of OSA in patients with CRC was identified as 16.17%, which is slightly higher than the 13.0% morbidity of OSA in the Chinese population. This slight difference could be attributed to the higher rates of smoking behavior (26.78%) and hypertension (22.39%) in these patients along with changes in sleep disturbance due to the clinical characteristics of intestinal tumor, thus increasing OSA morbidity. However, intestinal tumors

Table 2 Comparison of the general conditions of patients with CRC in different obstructive sleep apnea groups

Variables	Cases	ODI groups		Frequency/χ^2	P value
		ODI <5 (n=337)	ODI ≥5 (n=65)		
Gender				0.976	0.323
Male	225	185 (54.90)	40 (64.54)		
Female	177	152 (45.10)	25 (38.46)		
Age (years)	402	58.96±11.60	58.66±11.90	0.035	0.851
BMI	402	22.16±3.37	22.53±3.23	0.653	0.419
Smoking				0.601	0.438
Yes	108	31 (9.20)	8 (12.31)		
No	294	306 (90.80)	57 (87.69)		
Alcohol consumption				0.424	0.515
Yes	75	61 (18.10)	14 (21.54)		
No	327	276 (81.90)	51 (78.46)		
Hypertension				2.089	0.148
Yes	90	71 (21.07)	19 (29.23)		
No	312	266 (78.93)	46 (70.77)		
Diabetes mellitus				3.114	0.097
Yes	26	25 (7.42)	1 (1.54)		
No	376	312 (92.58)	64 (98.46)		
Coronary heart disease				0.301	0.583
Yes	45	39 (11.57)	6 (9.23)		
No	357	298 (88.43)	59 (90.77)		
Sleep monitoring stage				1.468	0.506
No surgery	67	56 (16.62)	11 (16.92)		
Surgery					
Pre-surgery	315	15 (4.45)	15 (7.69)		
Post-surgery	20	266 (78.93)	49 (75.38)		
TST (h)	402	5.49±1.26	5.01±1.31	15.949	<0.001
$MSaO_2$ (%)	402	95.66±2.50	92.89±3.10	62.623	<0.001
$LSaO_2$ (%)	402	81.30±8.06	78.82±7.73	5.227	0.023
Tsat90 (%)	402	6.11±14.53	20.54±19.62	47.526	<0.001
PSQI score	402	8.29±4.58	9.54±4.37	4.101	0.044

BMI, body mass index; ODI, oxygen desaturation index; $MSaO_2$, mean oxygen saturation; $LSaO_2$, lowest oxygen saturation; Tsat90, the percentage of night-time spent with oxygen saturation less than 90%, TST, total sleep time; PSQI, Pittsburgh Sleep Quality Index.

Table 3 Comparison of the clinicopathological characteristics of patients with CRC in different obstructive sleep apnea groups

Variables	Cases	ODI groups		F/χ^2	P value
		ODI <5 (n=337)	ODI ≥5 (n=65)		
Type of CRC				0.083	0.773
Colon cancer	223	188 (84.30)	35 (15.70)		
Rectal cancer	179	149 (83.24)	30 (16.76)		
Site of tumor origin				0.024	0.877
Left hemicolon	325	272 (83.69)	53 (16.31)		
Right hemicolon	77	65 (84.42)	12 (15.58)		
Pathological type				1.913	0.597
Non-adenocarcinoma	9	8 (88.89)	1 (11.11)		
Poorly differentiated adenocarcinoma	66	53 (80.30)	13 (19.70)		
Moderately differentiated adenocarcinoma	278	232 (83.46)	46 (16.55)		
Highly differentiated adenocarcinoma	49	44 (89.80)	5 (10.20)		
Tumor stage				2.356	0.507
Stage I	42	35 (83.33)	7 (16.67)		
Stage II	104	92 (88.46)	12 (11.54)		
Stage III	145	119 (82.07)	26 (17.93)		
Stage IV	109	89 (81.65)	20 (18.35)		
T-stage				1.394	0.715
T1	26	23 (88.46)	3 (11.54)		
T2	47	39 (82.98)	8 (17.02)		
T3	75	65 (86.67)	10 (13.33)		
T4	238	194 (81.51)	44 (18.49)		
N-stage				4.136	0.042
N0 + N1	218	261 (84.74)	47 (15.26)		
N2	71	53 (74.65)	18 (25.35)		
M-stage				0.136	0.762
M0	292	24 (84.25)	46 (15.75)		
M1	110	91 (82.73)	19 (17.27)		

CRC, colorectal cancer; T-stage, tumor stage; N-stage, node stage; M-stage, metastasis stage; ODI, oxygen desaturation index.

originate in the abdominal cavity and thereby do not significantly and directly affect the airway and pulmonary respiratory function.

Sleep disturbance is associated with common chronic diseases. Hypertension and CAD are associated with excessive or too short sleep duration (22,28) and are crucial factors in deteriorating the quality of life of patients with tumors (29,30). Compared to a 9% morbidity in the general population (31), the morbidity of sleep disorders in patients with tumors reaches an approximate high of between 30% (32) and 93.1% (33). There are significant differences in the sleep status of different tumor types. Treatment modalities such as chemotherapy and radiotherapy are important factors that cause sleep disturbance in patients

Table 4 Comparison between the colorectal cancer groups with different TNM stages [cases (%)]

Variables	T				P value	N		P value	M		P value
	T1	T2	T3	T4		N0+N1	N2		M0	M1	
Gender					0.049			0.889			0.147
Male	9 (4.21)	25 (11.68)	37 (17.29)	143 (66.82)		172 (55.84)	39 (54.93)		157 (53.77)	68 (61.82)	
Female	17 (9.88)	22 (12.79)	38 (22.09)	95 (55.23)		136 (44.16)	32 (45.07)		135 (46.23)	42 (38.18)	
Age (years)					0.203			0.014			0.002
<65	17 (65.38)	26 (55.32)	52 (69.33)	169 (71.01)		201 (77.91)	57 (22.09)		186 (67.88)	88 (32.12)	
≥65	9 (34.62)	21 (44.68)	23 (30.67)	69 (28.99)		107 (88.43)	14 (11.52)		106 (82.81)	22 (17.19)	
Hypertension					0.727			0.120			0.214
Yes	5 (19.23)	10 (21.28)	14 (18.67)	58 (24.37)		74 (24.03)	11 (15.49)		70 (23.97)	20 (18.18)	
No	21 (80.77)	37 (78.72)	61 (81.33)	180 (75.63)		234 (75.97)	60 (84.51)		222 (76.03)	90 (81.82)	
Coronary heart disease					0.874			0.773			0.340
Yes	2 (7.69)	4 (8.51)	9 (12.00)	27 (11.34)		34 (11.04)	7 (9.86)		30 (10.27)	15 (13.64)	
No	24 (92.31)	43 (91.49)	66 (88.00)	211 (88.66)		274 (88.96)	64 (90.14)		262 (89.73)	95 (86.36)	
Diabetes mellitus					0.649			0.591			0.157
Yes	3 (11.54)	2 (4.26)	5 (6.67)	14 (5.88)		21 (6.82)	3 (4.23)		22 (7.53)	4 (3.64)	
No	23 (88.46)	45 (95.74)	70 (93.33)	224 (94.12)		287 (93.18)	68 (95.77)		270 (92.47)	106 (96.36)	
Smoking					0.776			0.958			0.102
Yes	2 (7.69)	3 (6.38)	7 (9.33)	26 (10.92)		31 (10.06)	7 (9.86)		24 (8.22)	15 (13.64)	
No	24 (92.31)	44 (93.62)	68 (90.67)	212 (89.08)		277 (89.94)	64 (90.14)		268 (91.78)	95 (86.36)	
Alcohol consumption					0.136			0.665			0.032
Yes	3 (11.54)	7 (14.89)	9 (12.00)	53 (22.27)		54 (17.53)	14 (19.72)		47 (62.67)	28 (37.33)	
No	23 (88.46)	40 (85.11)	66 (88.00)	185 (77.73)		254 (82.47)	57 (80.28)		245 (74.92)	82 (25.08)	
BMI					0.445			0.352			0.270
<28 kg/m^2	25 (96.15)	43 (91.49)	71 (94.67)	230 (96.64)		293 (95.13)	69 (97.18)		278 (95.21)	107 (97.27)	
≥28 kg/m^2	1 (3.85)	4 (8.51)	4 (5.33)	8 (3.36)		15 (4.87)	2 (2.82)		14 (4.79)	3 (2.73)	
TST (h)	5.40±1.26	6.02±1.03	5.42±1.23	5.36±1.36	0.345	5.42±1.30	5.28±1.28	0.211	5.40±1.28	5.45±1.30	0.630
$MSaO_2$ (%)	95.29±2.82	95.69±1.85	95.68±2.37	94.94±3.10	0.136	95.22±2.75	94.96±3.28	0.491	95.23±2.69	95.15±3.07	0.803
$LSaO_2$ (%)	82.12±7.38	82.21±7.04	82.36±7.70	79.99±8.31	0.061	81.37±7.47	78.96±9.23	0.020	81.35±7.63	79.68±9.01	0.064
Tsat90 (%)	8.52±17.44	5.31±7.34	5.92±12.68	10.12±18.69	0.122	8.21±15.88	11.01±20.02	0.204	8.25±15.73	8.94±17.87	0.708
PSQI score	9.04±4.47	8.72±4.43	8.62±4.69	8.24±4.56	0.755	8.49±4.50	8.04±4.82	0.453	8.53±4.67	8.40±4.29	0.803

T, tumor; N, node; M, metastasis; BMI, body mass index; TST, total sleep time; $MSaO_2$, mean oxygen saturation; $LSaO_2$, lowest oxygen saturation; Tsat90, the percentage of night-time spent with oxygen saturation less than 90%, PSQI, Pittsburgh Sleep Quality Index.

with breast and cervical cancer (34,35); moreover, the lung cancer subtype has the worst sleep quality among various tumor subtypes and a complex type of sleep disturbance (33). As the tumor stage advances, patients with CRC show increasing tumor-related symptoms and sleep quality deterioration. The average TST for patients with CRC was found to be 5.41 hours, which is lower than the 7 hours of the general population, and physical anomalies caused by

Table 5 Analysis of factors influencing the N-stage in patients with CRC

Variables	B	SE	Wald	P value	OR	95% CI
ODI groups						
ODI <5					1 (ref)	
ODI ≥5	0.650	0.319	4.149	0.042	1.915	1.025–3.579
Age (years)						
<65	0.784	0.323	5.889	0.015	2.190	1.163–4.125
≥65					1 (ref)	
Constant	–3.605	0.719	25.173	0.000	0.027	

CRC, colorectal cancer; ODI, oxygen desaturation index; OR, odds ratio; CI, confidence interval; B, regression coefficient; SE, standard error.

bowel cancer remained the main influencing factor.

As a marker of OSA, IH could be a key factor influencing tumorigenesis and death (36). The IH is involved in tumor progression, including metabolism, proliferation, apoptosis, and angiogenesis via several mechanisms such as increasing gene mutation frequency (37), stimulating reactive free radical production (38) and promoting endothelial cell proliferation (37). Animal studies using lung cancer models have also shown that IH promotes cancer cell invasiveness (39,40) and increases melanoma cell growth, necrosis, and pulmonary metastasis (41). The earliest study in humans is the famous Wisconsin Sleep Cohort (42), where 1,522 patients from the community were followed up for an average of 22 years and the overall mortality rate for patients with OSA was 7.36%, with higher tumor mortality in patients with OSA (5.21%) than in those without OSA (2.68%). Currently, CRC is the second highest contributor to cancer-related deaths. A study by Huang *et al.* (43) on OSA and lung cancer mortality in 2020 showed that the severity of OSA is associated with an increased risk of death in patients with stage III and IV lung cancer. Additionally, a small population study showed that ODI is strongly associated with high renal cancer recurrence indicators, such as Breslow index, presence of ulcers, and mitotic index, in postoperative patients with renal clear cell carcinoma combined with OSA (27). Similarly, increased expression of hypoxia-inducible factor 1 (HIF-1) in patients with melanoma combined with OSA and IH was also associated with higher Fuhrman grading (44). Additionally, there is an association between high HIF-1 expression and metastasis in gynecological tumors, pancreatic cancer, and esophageal cancer (45-47). However, no correlation between OSA and clinicopathological characteristics has been observed in postmenopausal patients with breast and endometrial cancers, despite the high morbidity of OSA (48).

In this study, the main clinicopathological characteristics of patients with CRC, including tumor origin site, TNM stage, treatment modality, and pathological type were analyzed. The results showed no significant differences in gender, age, comorbidities, and sleep status between colon cancer and rectal cancer, left and right hemicolon cancer, and different pathological types, with TNM staging showing strong associations with morbidity and being the most crucial clinical indicator of survival and prognosis for patients with tumors. Patients with an ODI ≥5 had an increased risk of lymph node metastasis compared to those with an ODI <5. In a retrospective study of 1,031 patients with pancreatic ductal adenocarcinoma, the morbidity of negative lymph nodes was significantly higher in those with combined OSA than in those without OSA, which is an independent predictor of lymph node status (hazard ratio =0.051, P=0.038). Moreover, the overall survival in the combined OSA group was similar to that in the non-OSA group (49), which is inconsistent with our findings. Furthermore, an association between tumor size, distant metastasis, and OSA-related indicators, except for the lymph node stage, could not be found. Lymph node metastasis is a key indicator of malignant tumors, including CRC, and acts as a prognostic factor for OSA diagnosis. Understanding the association between OSA and clinicopathological characteristics, such as lymph node metastasis, requires further extensive study.

In this study, patients with post-surgical recovery of >1 month were included to reduce the interference of surgery with the sleep quality indicators of patients. However, significant differences in ODI and other sleep

indicators between pre-surgery, 1-month post-surgery, and non-surgery patients were not observed. Patients with CRC in the normal ODI group had a significantly longer TST than those in the abnormal ODI group. Moreover, patients with higher PSQI scores were at a higher risk of abnormal ODI. Furthermore, several other indicators related to OSA, such as $MsaO_2$, $LsaO_2$, and Tsat90 were not associated with pathological staging and tumor stage.

Highlights and limitations

To the best of our knowledge, this study was the first to screen OSA in patients with CRC to obtain sleep-related information. Due to the specificity of intestinal tumors and poor patient compliance, the wearable sleep monitoring device lacked information on AHI. Combined with previous studies, the results of this study suggest that the morbidity of OSA and its correlation with clinicopathological characteristics vary significantly in different types of tumors. Hence, it is necessary to carry out OSA screening in all tumor types to clarify their association. Additionally, a follow-up cohort will be used to investigate the correlation between OSA morbidity and CRC progression and survival status.

Conclusions

The prevalence of OSA is high in patients with CRC. The risk of lymph node metastasis in patients with CRC is associated with abnormal ODI, and patients with ODI ≥5 and aged ≥65 years have a higher risk of N2 tumor stage.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-175/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-175/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-175/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Huizhou Municipal Central Hospital Ethics Committee, and all participants signed informed consent.

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