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# Diagnostic value of circRNA-UBAP2 and CXCR4 mRNA expression combined with endoscopic ultrasonography in colorectal cancer

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► ***Original article***

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## ABSTRACT

***Background:*** To investigate the clinical value of combining the expression of circular RNA ubiquitin associated protein 2 (circRNA-UBAP2) and chemokine receptor 4 (CXCR4) messenger RNA（mRNA）with endoscopic ultrasonography for the diagnosis of colorectal cancer (CRC). ***Materials and Methods:*** A retrospective study was conducted. 104 patients with CRC and 87 patients with colorectal adenoma who were admitted to the hospital from May 2022 to May 2024 were enrolled in the study. The expression levels of circRNA-UBAP2 and CXCR4 mRNA in samples were detected. The relationship between the expression of circRNA-UBAP2 and CXCR4 mRNA and clinicopathological features of patients with CRC was analyzed, and the diagnostic efficacy of circRNA-UBAP2 and CXCR4 mRNA combined with endoscopic ultrasonography for CRC were evaluated. ***Results:*** The expression levels of circRNA-UBAP2 and CXCR4 mRNA in cancer tissues of patients with CRC were higher than those in adjacent tissues (P<0.05). Statistically significant differences in the expression levels of circRNA-UBAP2 and CXCR4 mRNA were observed among patients with different differentiation degrees, TNM stages, and lymph node metastasis status (P<0.05). The accuracy of endoscopic ultrasonography in diagnosing CRC was 87.96% (kappa value=0.758). The AUC (95% CI) of joint diagnosis was 0.980 (0.958-1.000), which was larger than that of separate diagnosis (P<0.05). ***Conclusion:*** circRNA-UBAP2 and CXCR4 mRNA are highly expressed in patients with CRC, and are associated with differentiation degree, TNM staging, and lymph node metastasis. The two are helpful in distinguishing CRC from colorectal adenoma, and their combination with endoscopic ultrasonography can improve diagnostic efficacy.

## INTRODUCTION

Colorectal cancer (CRC) is a common digestive tract tumor disease in clinical practice. Surgical resection can improve the survival rate of patients with early CRC, but most patients are already in the late stage when diagnosed. Due to the high metastasis and high recurrence of CRC, the prognosis of patients has not been significantly improved [1-3]. Ultrasound endoscopy is a commonly used imaging method for clinical diagnosis of CRC, but there are differences in the diagnostic accuracy of ultrasound endoscopy in different studies, and its effectiveness in differentiating CRC from lesions around colorectal tissue needs to be further improved [4]. In recent years, with the deepening of molecular biology research, molecular diagnosis based on biomarkers has gradually become a research hotspot for CRC diagnosis [5]. Studies on the pathogenesis of CRC [6] have found that the dysregulation of multiple signaling pathways caused by differential gene expression is an important factor leading to the malignant biological behavior of CRC tumor cells. Circular RNA ubiquitin *associated protein 2 (circRNA-UBAP2)* can bind to ubiquitinase to induce messenger RNA (*mRNA)* degradation and has become a highly promising tumor biomarker [7, 8]. Chemokine receptor 4 (CXCR4) is a classic receptor for cellular chemokines. Its overexpression contributes to the chemotaxis, proliferation, invasion and metastasis of tumor cells [9]. Recent studies [10] have shown that the epigenetic regulation of CXCR4 signaling may be related to certain specific *circRNAs*, which jointly participate in the biological behavior of tumors. Although *circRNA-UBAP2* and *CXCR4* may have functional associations in theory, their synergistic expression patterns and joint diagnostic value in CRC have not been systematically studied. Based on this, this study selected *circRNA-UBAP2* and *CXCR4. mRNA,* to investigate their expression levels in CRC and their relationship with patient pathological features. Furthermore, the authors further combined endoscopic ultrasound imaging features to evaluate the value of both alone and in combination in the differential diagnosis and assessment of CRC and surrounding colorectal lesions, hoping to provide new molecular imaging strategies for early diagnosis, precise staging, and personalized treatment of CRC.



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This study is innovative in that it combines *circRNA-UBAP2* with *CXCR4 mRNA* expression for the first time, integrating endoscopic ultrasound imaging features, aiming to improve the accuracy and reliability of CRC diagnosis.

## MATERIALS AND METHODS

### *Clinical data*

A retrospective study was conducted to collect data from CRC patients ($n$=104) and colorectal adenoma (CRA) patients ($n$=87) who were treated in our hospital from May 2022 to May 2024. The patients were included in the CRC group and the CRA group, respectively. Inclusion criteria: (1) Patients in the CRC group were diagnosed with CRC by postoperative pathological diagnosis [11] and underwent radical colorectal surgery. (2) Patients in the CRA group were diagnosed with CRA by colonoscopy biopsy [12]. (3) General clinical data and pathological examination data were complete. (4) Patients had sufficient specimens for testing. Exclusion criteria: (1) Patients who received relevant treatment before surgery. (2) Patients with other intestinal organic diseases or malignant tumors. (3) Patients with coagulation disorders or severe immunodeficiency. (4) Patients with acute or chronic infections. There were 66 males and 38 females in the CRC group, aged 32 to 78 years, with an average age of (53.46±8.79) years. The CRA group included 48 males and 39 females, aged 35 to 70 years (mean, 52.63±7.84 years). General information was comparable between the two groups ($P$>0.05).

### *Sample collection*

Cancer tissue and adjacent tissue 2–5 cm from the lesion margin were obtained during surgery from patients in the CRC group. CRA tissue samples were obtained from patients in the CRA group. Samples were immediately rapidly frozen in liquid nitrogen and stored at −80°C until use.

### *CircRNA-UBAP2* and *CXCR4 mRNA* expression

Tissue samples were collected and ground, and total RNA was extracted. cDNA was synthesized and amplified using a PCR kit (Qiagen, Germany) in a 7900HT PCR amplifier (Applied Biosystems, USA). Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as an internal control. Primer sequences (Shanghai Sangon Biotechnology Co., Ltd.) were: *circRNA-UBAP2:* upstream 5'-AGCCTAGAGCCAACTCCTTTG-3', downstream 5'-TCAGGTTGAGATTTGAAGTCAAGA-3'; *CXCR4 mRNA:* upstream 5'-TGGCCTTATCCTGCCTGGTAT-3', downstream 5'-GGAGTCGATGCTGATCCCAAT-3'. Expression levels were calculated using a $2^{-\Delta\Delta CT}$.

### *Endoscopic ultrasound*

Before the examination, routine bowel cleansing and oral defoaming agents were administered. The examination was performed using the EU-ME1 endoscopic ultrasound system (Olympus, Japan), with the UC-UCT260 (large probe) and UM-BS20-26R (small probe). The patient was positioned in the left lateral decubitus position. The endoscope was positioned and positioned to obtain clear ultrasound images, capturing information such as the lesion's size, location, morphology, and regional lymph node and adjacent organ metastases. A small probe was inserted through the working port, and water was injected into the intestinal lumen. Once the intestinal lumen was filled, an ultrasound scan was performed. The probe was aligned parallel to the lesion during the ultrasound scan, and the ultrasound frequency was set at 12 MHz. The extent of lesion invasion and local infiltration were observed. Diagnostic criteria for CRC: Lesions confined to layers 1 and 2 (mucosa and muscularis mucosae) on endoscopic ultrasound images are considered intramucosal carcinomas. Lesions that destroy layers 1 and 2 and invade layer 3 (submucosa) are considered submucosal carcinomas. Lesions that destroy layers 1 to 3 and cause irregular disruptions in layer 4 (muscularis propria) are considered muscularis propria carcinomas. Lesions that invade layer 5 (serosa) but have not yet invaded other organs are considered serosal carcinomas. Diagnostic criteria for CRA: On endoscopic ultrasound images, the lesion demonstrates papillary, finger-like, or dome-like echogenicity with clear, well-defined contours, protruding from the mucosa into the intestinal lumen, with clear and intact structures of all intestinal wall layers and no infiltration or destruction of the submucosal layer.

### *Observation indicators*

*CircRNA-UBAP2* and *CXCR4 mRNA* in CRC patients and CRA patients. (2) Analyze the relationship between *circRNA-UBAP2* and *CXCR4 mRNA* expression levels and pathological characteristics of CRC patients. (3) Analyze the diagnostic efficacy of endoscopic ultrasound in diagnosing CRC. (4) Analyze the diagnostic efficacy of *circRNA-UBAP2* and *CXCR4 mRNA* combined with endoscopic ultrasound in diagnosing CRC.

### *Statistical analysis*

SPSS 27.0 software was used for data analysis. The measurement data were expressed as ($\bar{x}\pm s$), and the independent sample $t$ test was used for comparison between groups. The count data were expressed as n (%) and the $\chi^2$ test was used, and the rank sum test was used for the graded data. The Kappa consistency test was used to analyze the consistency of the results of ultrasound endoscopy and pathological examination. The Spearman correlation analysis method was used for correlation analysis. The receiver operating characteristic (ROC) curve was used to analyze the diagnostic efficacy of


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circRNA-UBAP2, CXCR4 mRNA, and ultrasound endoscopy in diagnosing CRC, and the area under the curve (AUC) was compared by z test. Test level: α = 0.05.

## RESULTS

### *Expression of circRNA-UBAP2 and CXCR4 mRNA in CRC tissues*

Expression of *circRNA-UBAP2* and *CXCR4 mRNA* in CRC tissues were significantly higher than those in adjacent tissues ($P < 0.05$) (table 1).

**Table 1.** Expression of circRNA-UBAP2 and CXCR4 mRNA in CRC tissues ($\bar{x}$±s).

| Group | *circRNA-UBAP2* | *CXCR4 mRNA* |
|---|---|---|
| Cancer tissue (*n* = 104) | 2.29±0.57 | 0.57±0.12 |
| Peritumoral tissue (*n* = 104) | 1.08±0.21 | 0.19±0.05 |
| *t* | 20.314 | 29.810 |
| *P* | <0.001 | <0.001 |

Note: CRC: colorectal cancer. circRNA-UBAP2: circular RNA ubiquitin-associated protein 2. CXCR4 mRNA: chemokine receptor 4 mRNA.

### *Expression of circRNA-UBAP2 and CXCR4 mRNA in CRC and CRA patients*

Expression of *circRNA-UBAP2* and *CXCR4 mRNA* in CRC tissues were significantly higher than those in CRA patients ($P<0.05$) (table 2).

**Table 2.** Expression of circRNA-UBAP2 and CXCR4 mRNA in CRC and CRA patients ($\bar{x}$±s).

| Group | *circRNA-UBAP2* | *CXCR4 mRNA* |
|---|---|---|
| CRC group (*n* =104) | 2.29±0.57 | 0.57±0.12 |
| CRA group (*n* = 87) | 1.64±0.31 | 0.33±0.09 |
| *t* | 9.521 | 15.381 |
| *P* | <0.001 | <0.001 |

Note: CRC: colorectal cancer. CRA: colorectal adenoma. circRNA-UBAP2: circular RNA ubiquitin-associated protein 2. CXCR4 mRNA: chemokine receptor 4 messenger RNA.

### *Expression of circRNA-UBAP2 and CXCR4 mRNA and different pathological characteristics*

Expression of *circRNA-UBAP2* and *CXCR4 mRNA* was higher in poorly differentiated CRC patients than in well-differentiated patients, higher in stage III–IV patients than in stage I–II patients, and higher in patients with lymph node metastasis than in those without ($P<0.05$) (table 3).

### *Relationship between circRNA-UBAP2 and CXCR4 mRNA and pathological characteristics*

The degree of differentiation was negatively correlated with the expression of *circRNA-UBAP2* and *CXCR4 mRNA* ($P<0.05$). TNM stage and lymph node metastasis were positively correlated with the expression of *circRNA-UBAP2* and *CXCR4 mRNA* ($P<0.05$) (table 4).

### *Analysis of the value of endoscopic ultrasound in diagnosing CRC*

Endoscopic ultrasound detected 101 CRC cases and CRA 90 cases. The accuracy of CRC diagnosis was 87.96%, with sensitivity and specificity of 87.50% and 88.51%, respectively. The positive and negative predictive values were 90.10% and 95.56%, respectively. The kappa value of the concordance test with pathological diagnosis was 0.758 (table 5).

**Table 3.** Expression of circRNA-UBAP2 and CXCR4 mRNA in CRC patients with different pathological characteristics ($\bar{x}$±s).

| project | *n* | *circRNA-UBAP2* | *t* | *P* | *CXCR4 mRNA* | *t* | *P* |
|---|---|---|---|---|---|---|---|
| gender | | | 0.512 | 0.610 | | 1.197 | 0.234 |
| male | 66 | 2.31±0.59 | | | 0.58±0.13 | | |
| female | 38 | 2.25±0.55 | | | 0.55±0.11 | | |
| Age (years) | | | 0.614 | 0.540 | | 0.415 | 0.679 |
| <50 years old | 41 | 2.25±0.58 | | | 0.56±0.12 | | |
| ≥50 years old | 63 | 2.32±0.56 | | | 0.57±0.12 | | |
| Family history of CRC | | | 0.236 | 0.814 | | 0.231 | 0.818 |
| Yes | 8 | 2.34±0.52 | | | 0.58±0.08 | | |
| no | 96 | 2.29±0.58 | | | 0.57±0.12 | | |
| Tumor size (cm) | | | 1.172 | 0.244 | | 1.297 | 0.197 |
| <5 | 56 | 2.23±0.55 | | | 0.56±0.08 | | |
| ≥5 | 48 | 2.36±0.58 | | | 0.59±0.15 | | |
| Tumor location | | | 0.349 | 0.728 | | 1.630 | 0.106 |
| colon | 61 | 2.31±0.55 | | | 0.55±0.11 | | |
| rectum | 43 | 2.27±0.61 | | | 0.59±0.14 | | |
| Infiltration depth | | | 0.165 | 0.848 | | 0.616 | 0.542 |
| Serous layer and full layer | 83 | 2.31±0.58 | | | 0.58±0.11 | | |
| mucosal layer | 11 | 2.24±0.51 | | | 0.56±0.15 | | |
| Submucosa | 10 | 2.22±0.56 | | | 0.54±0.13 | | |
| Vascular invasion | | | 0.163 | 0.871 | | 0.401 | 0.689 |
| yes | 31 | 2.30±0.60 | | | 0.56±0.13 | | |
| no | 73 | 2.28±0.56 | | | 0.57±0.11 | | |
| Degree of differentiation | | | 3.169 | 0.002 | | 5.034 | <0.001 |
| poorly differentiated | 39 | 2.51±0.60 | | | 0.64±0.12 | | |
| Medium to high differentiation | 65 | 2.16±0.51 | | | 0.53±0.10 | | |
| TNM staging | | | 2.457 | 0.016 | | 2.598 | 0.011 |
| Stage I to II | 61 | 2.18±0.56 | | | 0.55±0.12 | | |
| Stage III-IV | 43 | 2.45±0.54 | | | 0.61±0.11 | | |
| Lymph node metastasis | | | 2.888 | 0.005 | | 3.107 | 0.003 |
| yes | 40 | 2.49±0.58 | | | 0.61±0.14 | | |
| no | 64 | 2.17±0.53 | | | 0.54±0.09 | | |

Note: CRC: colorectal cancer. circRNA-UBAP2: circular RNA ubiquitin-associated protein 2. CXCR4 mRNA: chemokine receptor 4 messenger RNA . TNM: tumor/regional lymph node/distant metastasis.

**Table 4.** Correlation between circRNA-UBAP2 and CXCR4 mRNA and pathological characteristics of CRC.

| project | *circRNA-UBAP2* | | *CXCR4 mRNA* | |
|---|---|---|---|---|
| | *r* | *P* | *r* | *P* |
| Degree of differentiation | -0.400 | <0.001 | -0.304 | 0.002 |
| TNM staging | 0.308 | 0.001 | 0.282 | 0.004 |
| Lymph node metastasis | 0.370 | <0.001 | 0.320 | <0.001 |

Note: CRC: colorectal cancer. circRNA-UBAP2: circular RNA ubiquitin-associated protein 2. CXCR4 mRNA: chemokine receptor 4 mRNA. TNM: tumor/regional lymph node/distant metastasis.



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**Table 5.** Analysis of the value of endoscopic ultrasound in the diagnosis of CRC.

| Endoscopic ultrasound | Pathological diagnosis | | total |
|---|---|---|---|
| | CRC | CRA | |
| CRC | 91 | 10 | 101 |
| CRA | 13 | 77 | 90 |
| total | 104 | 87 | 191 |

Note: CRC: colorectal cancer. CRA: colorectal adenoma.

### *Analysis of the value of circRNA-UBAP2 and CXCR4 mRNA and ultrasound endoscopy*

The results of ROC curve analysis showed that the AUCs of *circRNA-UBAP2, CXCR4 mRNA,* and endoscopic ultrasound for diagnosing CRC were 0.801, 0.948, and 0.880, respectively. The AUC of *circRNA-UBAP2* and *CXCR4 mRNA* combined with endoscopic ultrasound was 0.980, which was higher than that of each single indicator detection (Z=5.404, 1.886, and 3.973, *P*=<0.001, 0.043, and <0.001, respectively) (table 6 and figure 1).

**Table 6.** Analysis of the value of circRNA-UBAP2, CXCR4 mRNA, and endoscopic ultrasound in the diagnosis of CRC.

| index | AUC | 95% *CI* | *P* - value | Cutoff value | Youden Index | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|---|---|
| *circRNA-UBAP2* | 0.801 | 0.738~0.864 | <0.001 | 2.02 | 0.516 | 65.38 | 86.21 |
| *CXCR4 mRNA* | 0.948 | 0.920~0.977 | <0.001 | 0.43 | 0.779 | 89.42 | 88.51 |
| Endoscopic ultrasound | 0.880 | 0.834~0.926 | <0.001 | - | 0.760 | 87.50 | 88.51 |
| Combined diagnosis | 0.980 | 0.958~1.000 | <0.001 | - | 0.908 | 94.23 | 96.55 |

Note: CRC: colorectal cancer. circRNA-UBAP2: circular RNA ubiquitin-associated protein 2. CXCR4 mRNA: chemokine receptor 4 messenger RNA . AUC: area under the curve.

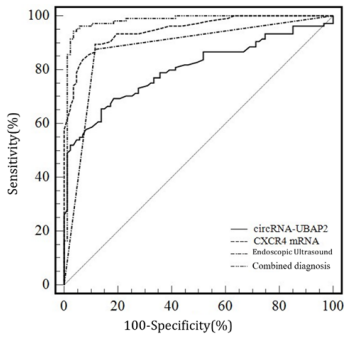


**Figure 1.** ROC curves of *circRNA-UBAP2, CXCR4 mRNA*, and endoscopic ultrasound for diagnosing CRC.

Figures 2 and 3 show Endoscopic ultrasound images of typical cases, a 66 years old female and a 58 years old male with detailed description of the images.

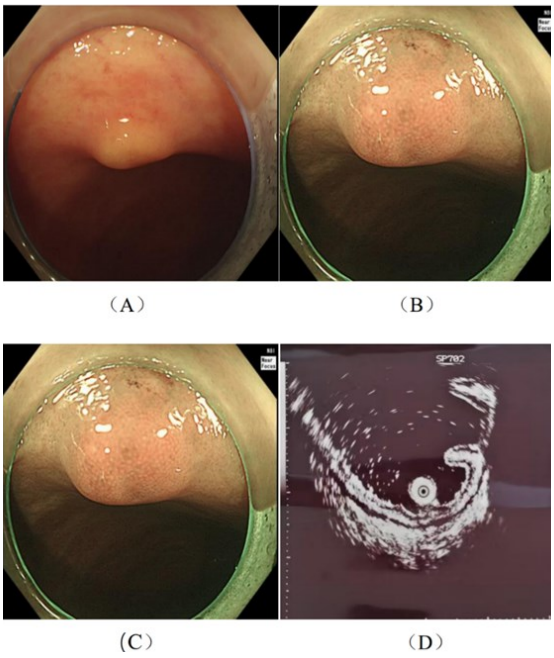


**Figure 2.** A 66-year-old female patient presented with complaints of intermittent, unformed bowel movements for 5 years. Pathological diagnosis was a low-grade neuroendocrine tumor. **(A)** A submucosal bulge, approximately 1.0 x 1.0 cm in size, with a smooth, yellowish surface, was observed approximately 5 cm from the anal verge. **(B)** NBI combined with magnifying endoscopy revealed a regular surface microstructure. **(C)** Endoscopic ultrasound revealed a hypoechoic structure, approximately 32 x 59 mm, with a poorly defined demarcation from the muscularis propria. **(D)** Endoscopic mucosal resection specimen.

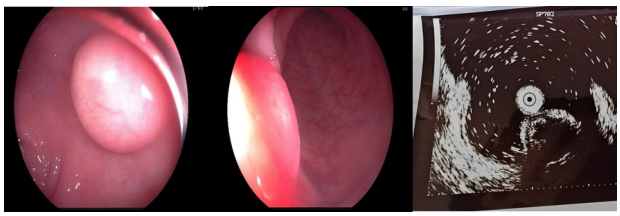

**Figure 3.** A 58- year-old male patient complained of intermittent, unformed bowel movements for two months. Pathologically diagnosed with a rectal space-occupying lesion (rectal carcinoid, G1). **(A, B)** Endoscope insertion 4 cm from the anus revealed a 1.2 x 1.5 mm mucosal bulge. The surface was smooth, with small, slightly yellowish-white depressions visible. The texture was firm to the touch. **(C)** Insertion of the ultrasound probe revealed intact mucosa at the bulge, with an anechoic mass visible in the submucosal layer. The submucosal area had clear boundaries, measuring approximately 7.1 x 11 mm in cross-section, and appeared partially connected to the muscularis propria.



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## DISCUSSION

The mortality rate of CRC ranks high among common malignant tumors in the world, and has shown a significant upward trend in recent years [13]. The survival rate of patients with early CRC after tumor resection is high, while the 5-year survival rate of patients with locally advanced CRC is only about 27% to 58% after surgery. Therefore, early diagnosis of CRC and timely intervention are of great significance to improving patient survival [14]. Ultrasound endoscopy uses tomography to display the structure of each layer of the digestive tract wall and can be used for early diagnosis of CRC. However, the operation of ultrasound endoscopy is relatively complex, and the diagnostic results are easily affected by factors such as equipment, operator experience, and lesion classification. There is still room for improvement in the diagnostic accuracy.

Currently, different studies have shown the role of non-coding RNAs such as miRNA, long non-coding RNA, and circRNA in tumor diseases. Among them, circRNA can bind to target miRNA, mediate the differentiation and metastasis of tumor cells, and thus affect the progression of tumor diseases. *CircRNA-UBAP2* not only plays a role in preeclampsia, but is also abnormally expressed in a variety of malignant tumors [15]. CXCR4 has the function of regulating tumor immunity and angiogenesis, and related studies have confirmed that high expression of CXCR4 is associated with the occurrence and distant metastasis of a variety of tumor diseases [16]. Clarifying the expression status of *circRNA-UBAP2* and CXCR4 in CRC may provide more reference for improving the accuracy of ultrasound endoscopy in diagnosing CRC.

This study found that *circRNA-UBAP2* and *CXCR4 mRNA* were highly expressed in CRC cancer tissues. The reason for this may be that the abnormally high expression of *circRNA-UBAP2* can regulate the miR-199a/vascular endothelial growth factor A axis, thereby promoting the invasion of CRC tumor cells [17]. The study by Li *et al*. [18] also confirmed that the high expression of *circRNA-UBAP2* may be related to the occurrence of CRC. CXCR4 can induce angiogenesis by recruiting endothelial progenitor cells, increasing the expression of vascular endothelial growth factor, and regulating the CXCL12 -CXCR4 signaling pathway [19]. In addition, abnormal expression of CXCR4 is associated with epithelial-mesenchymal transition, which can enhance the invasive ability of tumor cells [20]. The study by Nagasawa *et al.* [21] also confirmed that the expression level of *CXCR4 mRNA* was significantly increased in CRC cancer tissues.

This study further found that the expression levels of *circRNA-UBAP2* and *CXCR4 mRNA in CRC patients* were associated with some clinical pathological characteristics. *CircRNA-UBAP2* can competitively bind to miR-582-5p through the ceRNA mechanism, participate in regulating the expression of miR-582-5p target gene forkhead box protein O1 and its downstream signaling molecules, and promote tumor cell metastasis and epithelial-mesenchymal transition through the autophagy mechanism [22]. In the CRC mouse model, after blocking CXCR4 expression, the invasion and metastasis ability of tumor cells was significantly inhibited, which is considered to be related to CXCR4 inducing PI3K/AKT signaling pathway phosphorylation [23]. In this study, there was no statistical difference in the expression levels *of CXCR4* mRNA in patients with different tumor sizes, which is different from the results of previous studies [24]. It is considered that this may be related to individual differences in patients, small sample size, and different tumor locations.

Endoscopic ultrasound is used to perform preoperative diagnosis of CRC patients, which is helpful in guiding the clinical selection of appropriate treatment methods. The results of this study found that the consistency test between endoscopic ultrasound diagnosis of CRC and pathological diagnosis results was high, and the accuracy rate of CRC diagnosis was higher than 85%. Ma *et al*. [25] also found that endoscopic ultrasound can achieve a high preoperative diagnostic accuracy rate for the clinical diagnosis of CRC. However, some studies [26] believe that endoscopic ultrasound is based on the subjective judgment of the operator, which may lead to a decrease in diagnostic consistency. In addition, different histological types also affect the diagnostic accuracy to a certain extent. This study combined endoscopic ultrasound with *circRNA-UBAP2* and *CXCR4 mRNA* expression detection. The results showed that the AUC of *circRNA-UBAP2, CXCR4 mRNA,* and endoscopic ultrasound combined diagnosis was higher than that of a single indicator, indicating that the combined diagnosis of *circRNA-UBAP2, CXCR4 mRNA* expression and endoscopic ultrasound diagnosis has a higher diagnostic efficacy in CRC diagnosis. The combined detection has an amplification effect and can diagnose CRC more sensitively. Therefore, it has a better effect on the evaluation of patient disease than a single indicator.

*CircRNA-UBAP2* and *CXCR4 mRNA expression* in CRC tissues are associated with tumor differentiation, disease stage, and lymph node metastasis. *CircRNA-UBAP2* and *CXCR4 mRNA* expression have potential applications in the differential diagnosis of CRC and CRA, and combined with endoscopic ultrasound (EUS) can improve diagnostic efficacy.

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## REFERENCES


1. Baidoun F, Elshiwy K, Elkeraie Y, *et al*. (2021) Colorectal cancer epidemiology: Recent trends and impact on outcomes. *Curr Drug Targets,* ***22****(9): 998-1009*.
2. Luo X, Chen Y, Yang J, *et al.* (2024) Effect of additional surgical treatment on the prognosis of patients with high-risk T1 colorectal cancer undergoing endoscopic resection. *Journal of Sichuan University (Medical Edition),* ***55****(2): 411-417*.
3. Patel SG, Karlitz JJ, Yen T, *et al*. (2022) The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection. *Lancet Gastroenterol Hepatol,* ***7****(3): 262-274.*
4. Li R, Zhang Q, Xing J, *et al*. (2023) Analysis of the diagnostic value of endoscopic ultrasound for early colorectal cancer. *Journal of Capital Medical University,* ***44****(1): 126-130*.
5. Zou S, Huang Y, Yang Z, *et al*. (2024) NSUN2 promotes colorectal cancer progression by enhancing SKIL mRNA stabilization. *Clin Transl Med,* ***14****(3): e1621*.
6. Li J, Ma X, Chakravarti D, *et al*. (2021) Genetic and biological hallmarks of colorectal cancer. *Genes Dev,* ***35****(11-12): 787-820.*
7. Lv Z, Shi Y, Wu H, *et al*. (2024) Novel circular RNA CircUBAP2 drives tumor progression by regulating the miR-143/TFAP2B axis in prostate cancer. *Protein Pept Lett,* ***31****(1): 61-73.*
8. Xu Q, Deng B, Li M, *et al*. (2020) circRNA-UBAP2 promotes the proliferation and inhibits apoptosis of ovarian cancer though miR-382-5p/PRPF8 axis. *J Ovarian Res,* ***13****(1): 81*.
9. Yang Y, Li J, Lei W, *et al*. (2023) *CXCL12-CXCR4/CXCR7* axis in cancer: from mechanisms to clinical applications. *Int J Biol Sci,* ***19*** *(11): 3341-3359.*
10. Dong J, Xia R, Zhang Z, *et al*. (2021) lncRNA *MEG3* aggravated neuropathic pain and astrocyte overaction through mediating *miR-130a-5p/CXCL12/CXCR4* axis. *Aging,* ***13****(19): 23004-23019.*
11. National Health Commission of the People's Republic of China. Chinese Guidelines for the Diagnosis and Treatment of Colorectal Cancer (2023). *Chinese Journal of Digestive Surgery,* ***22****(6): 667-698*.
12. Hui Y, Zhao S, Ling T, *et al*. (2023) Guidelines for the prevention and treatment of colorectal adenoma with integrated traditional Chinese and Western medicine. *China Journal of Traditional Chinese Medicine,* ***48****(23): 6269-6277*.
13. Wu M, Gu K, Wu C, *et al*. (2023) Epidemic trends and age-period-cohort analysis of colorectal cancer in Shanghai from 1973 to 2017. *Oncology,* ***43****(4): 325-336*.
14. Dekker E, Tanis PJ, Vleugels JLA, *et al*. (2019) Colorectal cancer. *Lancet,* ***394****(10207): 1467-1480.*
15. Qi T, Zhang D, Shi X, *et al*. (2021) Decreased circUBAP2 expression is associated with preeclampsia by limiting trophoblast cell proliferation and migration. *Reprod Sci,* ***28****(8): 2237-2245*.
16. Alsayed RKME, Khan AQ, Ahmad F, *et al*. (2022) Epigenetic regulation of *CXCR4* signaling in cancer pathogenesis and progression. *Semin Cancer Biol,* ***22****(2): 697-708.*
17. Dai J, Zhuang Y, Tang M, *et al*. (2020) CircRNA *UBAP2* facilitates the progression of colorectal cancer by regulating miR-199a/VEGFA pathway. *Eur Rev Med Pharmacol Sci,* ***24****(15): 7963-7971.*
18. Li J, Yu L, Ma X, *et al.* (2023) Expression of circRNA UBAP2 in colorectal cancer and its effect on chemotherapy. *Journal of Gastroenterology and Hepatology,* ***32****(7): 752-755*.
19. Wang S, Luo J, Istvan B (2022) Biological functions of *CXCL12-CXCR4* in human malignant tumors. *Chinese Journal of Biochemistry and Molecular Biology,* ***38****(5): 577-586*.
20. Ahn S, Saha A, Clark R, *et al*. (2022) CXCR4 and CXCR7 signaling promotes tumor progression and obesity-associated epithelial-mesenchymal transition in prostate cancer cells. *Oncogene,* ***41*** *(41): 4633-4644.*
21. Nagasawa S, Tsuchida K, Shiozawa M, *et al*. (2021) Clinical significance of chemokine receptor *CXCR4* and *CCR7* mRNA expression in patients with colorectal cancer. *Anticancer Res,* ***41*** *(9): 4489-4495.*
22. Chen F, Guo L, Di J, *et al*. (2021) Circular RNA ubiquitin-associated protein 2 enhances autophagy and promotes colorectal cancer progression and metastasis via miR-582-5p/FOXO1 signaling. *J Genet Genomics,* ***48****(12): 1091-1103.*
23. Guan S, Yang R, Wu S, *et al*. (2022) The CD133+CXCR4+ colorectal tumor cells promote colorectal cancer progression by PI3K/AKT signaling. *J Interferon Cytokine Res,* ***42****(5): 195-202.*
24. Li T, Xu L, Li S, *et al.* (2020) Correlation between miR-126 expression level and CXCR4 and clinicopathological characteristics of patients with rectal cancer. *Chinese Journal of Gerontology,* ***40*** *(10): 2054-2057*.
25. Ma R and Lv Y (2021) Analysis of the value of endoscopic ultrasound in the preoperative diagnosis of high-grade intraepithelial neoplasia of colorectal mucosa. *Chinese Journal of Anorectal Diseases,* ***41****(2): 16-18.*
26. Li R, Zhang Q, Xing J, *et al*. (2023) Analysis of the diagnostic value of endoscopic ultrasound for early colorectal cancer. *Journal of Capital Medical University,* ***44****(1): 126-130*.




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