高危结直肠腺瘤的危险因素分析:聚焦非酒精性脂肪性肝病与多种代谢异常

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【摘要】 目的 回顾性分析代谢因素与高危结直肠腺瘤(colorectal adenoma,CRA)之间的关系。**方法** 收集2000年7月至2017年3月在新疆克拉玛依市中心医院首次接受结直肠镜检查的18~75岁患者的病历资料。采用非配对t检验比较结直肠镜正常(normal colonoscopy,NC)和高危CRA患者之间的差异,分类差异则使用χ^2检验。通过最小绝对收缩和选择算子(least absolute shrinkage and selection operator,LASSO)回归和Logistic回归分析影响高危CRA的代谢相关因素。**结果** 共纳入1 798例符合标准的病例,其中NC组972例,高危CRA组826例。高危CRA组高密度脂蛋白胆固醇(high-density lipoprotein cholesterol,HDL-C)水平显著低于NC组,而尿酸和肝纤维4因子(fibrosis 4,FIB-4)指数水平显著高于NC组(P均<0.05)。基于LASSO回归分析筛选出12个与高危CRA发生相关的变量,分别是年龄、性别、吸烟史、饮酒史、非酒精性脂肪性肝病(non-alcoholic fatty liver disease,NAFLD)、高血压、冠状动脉粥样硬化性心脏病、高血糖、高总胆固醇血症、低HDL-C血症、高水平谷丙转氨酶和高水平γ-谷氨酰转肽酶。Logistic回归分析提示,年长(≥50岁)、男性、吸烟史、饮酒史、低HDL-C血症、NAFLD和高血压史是高危CRA的独立危险因素(P<0.05)。在未校正和校正年龄、性别、吸烟、饮酒史4个变量的情况下,高TG/HDL-C比值(≥2.68)的患者发生高危CRA的风险显著高于低TG/HDL-C比值(<2.68)的患者(OR分别为1.430和1.235,P均<0.05);在未校正和校正变量的情况下,FIB-4指数>2.67的NAFLD患者发生高危CRA的OR分别为1.849和1.435(P=0.466、0.707)。**结论** 代谢因素与高危CRA之间存在显著关联。年长(≥50岁)、男性、吸烟史、饮酒史、低HDL-C血症、NAFLD和高血压史是高危CRA的独立危险因素;高TG/HDL-C比值(≥2.68)的患者发生高危CRA的风险显著增加。提示代谢异常的老年男性可能是结直肠镜筛查的重点人群。

【关键词】 代谢性疾病; 非酒精性脂肪性肝病(NAFLD); 结直肠腺瘤(CRA); 回顾性研究

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Analysis of risk factors for high-risk colorectal adenoma: focusing on non-alcoholic fatty liver disease and multiple metabolic abnormalities

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【Abstract】 **Objective** To retrospectively analyze the association between metabolic factors and high-risk colorectal adenoma (CRA). **Methods** The medical records of patients aged 18-75 years who underwent their initial colonoscopy at Karamay Central Hospital of Xinjiang Uygur Autonomous Region from Jul 2000 to Mar 2017 were collected. The comparison between normal colonoscopy (NC) and high-risk CRA patients was conducted using an unpaired *t*-test, while chi-square test was used for categorical variables. Least absolute shrinkage and selection operator (LASSO) regression and Logistic regression were utilized to analyze the association between metabolic factors and high-risk CRA. **Results** A total of 1 798 patients meeting the inclusion and exclusion criteria were enrolled and divided into normal colonoscopy (NC) findings group (n=972) and high-risk CRA group (n=826). The high-risk CRA group exhibited significantly lower levels of high-density lipoprotein cholesterol (HDL-C) in comparison to the NC group, while uric acid and fibrosis 4 (FIB-4) index levels were significantly higher than those observed in the NC group (all $P<0.05$). Based on LASSO regression analysis, we identified 12 variables that potentially influence the occurrence of high-risk CRA, including age, gender, smoking history, alcohol consumption history, non-alcoholic fatty liver disease (NAFLD), hypertension, coronary artery disease, hyperglycemia, hypercholesterolemia, low levels of HDL-C, elevated alanine aminotransferase, and elevated gamma-glutamyl transferase. Multivariate analysis revealed that individuals aged over 50 years, male gender, cigarette and alcohol consumption, low HDL-C levels, history of NAFLD and hypertension were identified as independent risk factors associated with high-risk CRA ($P<0.05$). In addition, without or with adjusting for age, sex, smoking, and drinking history, patients with a high TG/HDL-C ratio (the ratio$\geqslant$2.68) had a significantly higher risk of high-risk CRA than those with a low TG/HDL-C ratio (the ratio$<$2.68) [odds ratios (ORs) were1.430 and 1.235 respectively, all $P<0.05$)]. Without or with adjusting variables, the ORs for NAFLD patients with FIB-4 index$>$2.67 were 1.849 (P=0.466) and 1.435 (P=0.707), respectively. **Conclusion** A significant association exists between metabolic factors and high-risk CRA. Independent risk factors for high-risk CRA include older age ($\geqslant$50 years), male, smoking history, alcohol consumption history, low levels of HDL-C, and a history of NAFLD and hypertension. Individuals exhibiting a TG/HDL-C ratio exceeding 2.68 manifest a significantly heightened susceptibility to the development of high-risk CRA. Therefore, elderly males with one or more aforementioned metabolic abnormalities should be considered a priority population for colorectal screening.

【Key words】 metabolic disease; non-alcoholic fatty liver disease (NAFLD); colorectal adenoma (CRA); retrospective study

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结直肠癌(colorectal cancer,CRC)作为最常见的消化道恶性肿瘤[1-2]正呈现出患者年轻化的趋势[1]。由于晚期CRC的手术和药物治疗效果不佳，其疾病负担持续加重。结直肠腺瘤(colorectal adenoma,CRA)是CRC的癌前病变[3]，通过有效的结直肠镜检查及内镜下治疗腺瘤性息肉可显著降低其发病率。2020年，欧洲胃肠道内镜学会(European Society of Gastrointestinal Endoscopy,ESGE)发布的关于结直肠息肉切除术后的结直肠镜检查监测建议[4]指出，低风险腺瘤切除后不需要进一步的内镜监测，而高风险腺瘤则建议在3年后随访结直肠镜检查。考虑到结直肠镜检查具有侵入性、在部分地区普及度不足以及费用较高等问题，筛选出高危CRA人群显得尤为重要。

随着生活方式改变、工作压力增加以及锻炼时间减少，代谢功能障碍日益普遍化，导致2型糖尿病(type 2 diabetes mellitus,T2DM)和非酒精性脂肪性肝病(non-alcoholic fatty liver disease,NAFLD)等代谢性疾病增加，也与结直肠肿瘤(colorectal neoplasia,CRN)等多种肿瘤的发生密切相关[5-8]。

其他常见代谢性疾病如冠状动脉粥样硬化性心脏病(以下简称“冠心病”)(coronary artery disease, CAD)[9]、高血压(hypertension, HBP)[10]和高尿酸血症(hyperuricemia)[11]也被认为是CRA的危险因素。

目前鲜有研究探讨代谢因素与高危CRA之间的相关性。本研究筛选首次接受结直肠镜检查的门诊和住院患者的资料进行回顾性研究,旨在探究常见代谢相关因素对高危CRA的影响。

资料和方法

研究对象 纳入标准:(1)2000年7月至2017年3月在新疆克拉玛依市中心医院首次接受结直肠镜检查的患者;(2)内镜下结直肠黏膜无异常,或结直肠镜提示息肉(或内镜下行息肉摘除)且病理提示CRA;(3)年龄18~75岁。

排除标准:(1)存在结直肠恶性肿瘤或其他部位恶性肿瘤病史者;(2)存在其他结直肠疾病(如炎症性肠病、黏膜下病变、遗传性息肉病等)者;(3)有结直肠手术史者;(4)肠道准备差、影响视野者;(5)难以耐受、结直肠镜未达回盲部者;(6)其他肝病(包括慢性乙肝、过度饮酒等);(7)资料不完整者。

本研究经过新疆克拉玛依市中心医院伦理审查委员会批准,并豁免患者知情同意。

资料收集 收集病历中的基本信息如唯一号、性别、年龄、HBP史、T2DM史、CAD史、高尿酸血症史(痛风史包含在内)、高脂血症史、吸烟和饮酒史;收集血清学指标,包括空腹血糖(fasting blood glucose, FBG)、尿酸(uric acid, UA)、甘油三酯(triglyceride, TG)、总胆固醇(total cholesterol, TC)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、谷丙转氨酶(alanine aminotransferase, ALT))、谷草转氨酶(aspartate aminotransferase, AST)、碱性磷酸酶(alkaline phosphatase, ALP)、γ-谷氨酰转肽酶(gama-glutamyl transpeptidase, GGT);收集结直肠镜及病理组织学报告,CRA患者另外收集病灶的直径和数量。

高危结直肠腺瘤的诊断及评估 检查和病理学评估:结直肠镜检查由资深消化内科医师进行操作,使用直径5 mm活检钳评估每个息肉的大小。结直肠病变的组织学评估由对患者状态不知情、有经验的病理医师进行。高危CRA定义[4]:1个腺瘤≥10 mm或伴有高度异型增生,或≥5个腺瘤,或任何≥10 mm或伴有异型增生的锯齿状息肉。根据结直肠镜检查结果将患者分为结直肠镜检查正常(normal colonoscopy, NC)组和高危CRA组。

NAFLD的诊断[12-14]和评估[15] NAFLD的诊断标准:(1)无饮酒史或男性每日乙醇摄入量<30 g,女性<20 g[乙醇摄入量(g)=饮酒量(mL)×酒精度数(%)×0.8];(2)排除药物和其他病因导致的继发性脂肪肝;(3)存在弥漫性肝细胞脂肪变的影像学或组织学证据。使用肝纤维4因子(fibrosis 4, FIB-4)指数进行评估:

$$\text{FIB-4}=\frac{\text{年龄(岁)}\times \text{AST(U/L)}}{\text{血小板}(10^9/\text{L})\times \sqrt{\text{ALT}\ (\text{U/L})}}。$$

对于NAFLD,2级以下或3~4级以上的肝纤维化临界指分别为<1.3和>2.67[16];本研究以2.67为界来定义NAFLD肝纤维化的严重程度。

异常代谢指标的选择和定义 本研究重点关注代谢因素与高危CRA的相关性,将以下10项代谢指标纳入研究并定义如下:(1)高血糖、高TG和低HDL-C血症的定义参考我国代谢综合征[16]的诊断标准,即FBG≥110 mg/dL (6.1 mmol/L),高TG≥150 mg/dL (1.7 mmol/L),低HDL-C(男性)≤40 mg/dL (1.04 mmol/L);(2)高TC、高LDL-C和高UA血症的定义参考中国2型糖尿病防治指南(2020年版)[16],即高TC>200 mg/dL (>5.2 mmol/L)或口服他汀类药物,高LDL-C>130 mg/dL (>3.4 mmol/L)或口服他汀类药物,UA> 420 μmol/L或口服降尿酸药物;(3)高ALT、高AST和高ALP的定义参考中国2型糖尿病防治指南(2020年版)[16],即高ALT和高AST水平>40 U/L,高ALP>160 U/L;(4)高GGT的定义参考医院实验室检测上限(45 U/L)。

胰岛素抵抗的评估 TG/HDL-C比值也被用来评估胰岛素抵抗[17]。考虑到TG/HDL-C比值在不同人群中存在差异,我国安徽合肥的一项研究[18]发现,TG/HDL-C比值预测胰岛素抵抗的阈值为2.68。本研究中,TG/HDL-C比值≥2.68时认为存在胰岛素抵抗。

统计学分析 采用Shapiro-Wilk正态性检验判

断数据是否符合正态分布。若数据符合正态分布，连续变量以$\bar{x}\pm s$呈现，两组间比较采用非配对t检验；若数据不符合正态分布，则以M(P_{25}，P_{75})呈现，两组间比较采取秩和检验。分类变量总结为频数和构成比，采取χ^2检验比较分类差异。最小绝对收缩和选择算子(least absolute shrinkage and selection operator，LASSO)回归分析用于筛选高危CRA的代谢相关因素。将LASSO回归分析中有统计学差异的变量纳入Logistic回归模型进行多因素分析，结果以比值比(odds ratio，OR)和95%CI示。所有P值均为双侧，$P<0.05$为差异有统计学意义。LASSO回归分析采用R软件(4.4.0版)进行分析，其他统计分析使用SPSS 26.0软件。

结　　果

基线特征　本研究纳入符合纳排标准的病例共1 798例(图1)，其中男性患者863例(48.00%)。患者年龄18～75岁，平均(55.44±10.70)岁。依据结直肠镜检查结果和2020年ESGE发布的关于结直肠息肉切除术后结直肠镜检查监测的建议[4]，972例诊断为结直肠镜正常(normal colonoscopy，NC)，826例为高危CRA。高危CRA组的平均年龄显著高于NC组[(57.76±10.06)岁 *vs.* (53.47±10.84)岁，$t=-8.647$，$P<0.001$]，且高危CRA组男性患者占比显著高于NC组(54.48% *vs.* 42.49%，$\chi^2=25.718$，$P<0.001$)。

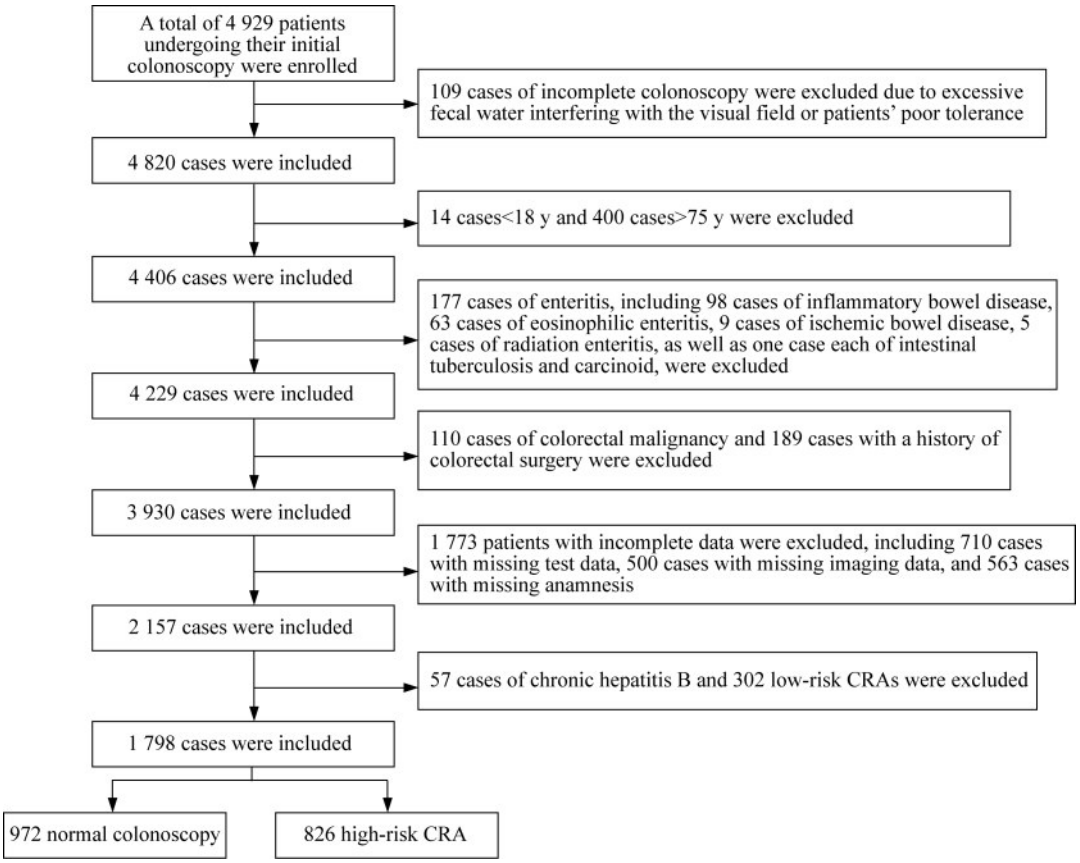


图1　患者入组流程图

Fig 1　Flowchart for patient selection

NC组和高危CRA组代谢指标　NC组和高危CRA组不同代谢指标的水平见表1。高危CRA组HDL-C水平显著低于NC组[(1.21±0.30)mmol/L *vs.* (1.30±0.36) mmol/L，$t=5.878$，$P<0.001$]。高危CRA组患者的UA水平显著高于NC组[(303.03±81.66) μmol/L *vs.*(286.48±80.63) μmol/L，$t=-4.312$，$P<0.001$)。FIB-4指数水平也显著高于NC组(1.35±0.68 *vs.* 1.24±0.74，$t=-3.228$，$P=0.001$)。

影响高危CRA的代谢因素的单因素分析　本研究中，年龄、性别、吸烟史、饮酒史、NAFLD史、HBP史、CAD史、高血糖、高UA血症、高TG血症、高TC血症、低HDL-C血症、高LDL-C血症、高

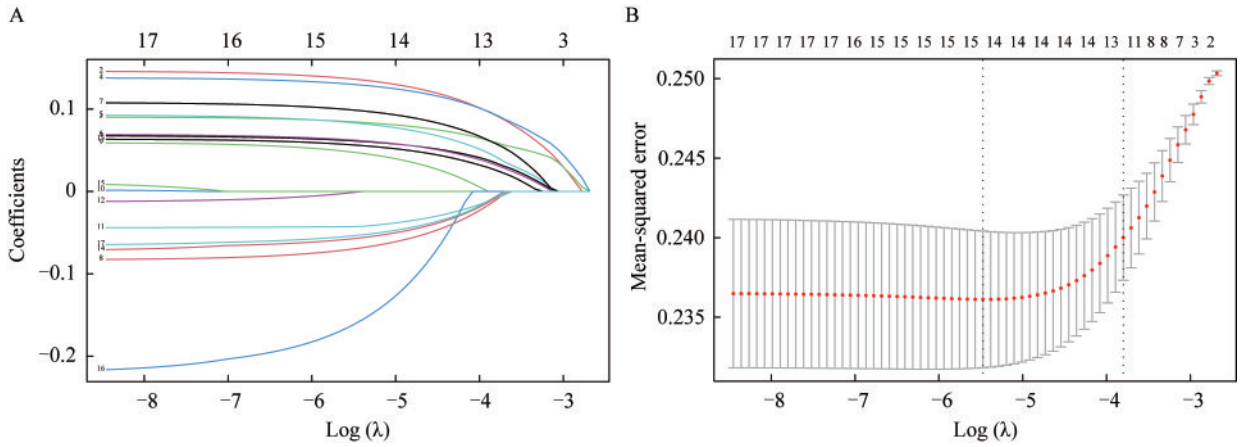
表1 NC组和高危CRA组不同代谢指标水平比较

Tab 1 Levels of various metabolic indicators in the normal colonoscopy and high-risk CRA groups ($\bar{x}\pm s$)

Indicators	Total (n=1 798)	NC (n=972)	High risk CRA (n=826)	t	P
FBG (mmol/L)	5.33±1.48	5.35±1.53	5.31±1.42	0.540	0.589
TG (mmol/L)	1.61±1.12	1.58±1.14	1.64±1.09	−1.248	0.212
TC (mmol/L)	4.54±1.00	4.57±0.97	4.51±1.03	1.235	0.217
HDL-C (mmol/L)	1.26±0.34	1.30±0.36	1.21±0.30	5.878	**<0.001**
LDL-C (mmol/L)	2.69±0.76	2.67±0.74	2.72±0.77	−1.324	0.186
UA (μmol/L)	294.08±81.50	286.48±80.63	303.03±81.66	−4.312	**<0.001**
ALT (U/L)	23.84±29.79	24.59±33.25	22.97±25.11	1.151	0.25
AST (U/L)	22.24±17.97	22.89±21.96	21.48±11.63	1.661	0.097
GGT (U/L)	26.73±39.82	26.49±38.37	27.01±41.49	−0.273	0.785
ALP (U/L)	65.44±22.89	65.99±24.53	64.78±20.81	1.138	0.255
FIB-4 index	1.29±0.71	1.24±0.74	1.35±0.68	−3.228	**0.001**
TG/HDL-C ratio	3.37±3.68	3.27±4.06	3.48±3.17	−1.177	0.239

NC: Normal colonoscopy; CRA: Colorectal adenoma; FBG: Fasting blood glucose; TG: Triglyceride; TC: Total cholesterol; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; UA: Uric acid; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gama-glutamyl transpeptidase; ALP: Aalkaline phosphatase; FIB-4: Fibrosis 4; TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol.

ALT、高AST、高ALP和高GGT为研究变量,纳入LASSO回归分析后筛选出12个具有非零系数特征、并通过交叉验证的变量,包括年龄、性别、吸烟、饮酒、NAFLD、HBP、CAD、高血糖、高TC血症、低HDL-C血症、高ALT和高GGT(图2)。



A: The LASSO regression coefficient path map of 17 variables was generated according to the log (λ) sequence of penalty variables, and 12 variables with non-zero coefficient characteristics were screened out. B: 10-fold cross-validation was used to validate the LASSO regression model.

图2 基于LASSO回归分析筛选出影响高危CRA发生的变量

Fig 2 LASSO regression analysis was used to screen variables affecting the occurrence of high-risk colorectal adenoma

影响高危CRA的代谢因素的多因素分析 将LASSO回归分析中具有统计学差异的指标纳入多因素Logistic回归分析,结果显示:年长(≥50岁)、男性、吸烟史、饮酒史、低HDL-C血症、有NAFLD和HBP史是高危CRA的独立危险因素(表2)。

胰岛素抵抗与高危CRA的相关性 采用TG/HDL-C比值评估胰岛素抵抗的情况,当TG/HDL-C比值≥2.68时认为存在胰岛素抵抗[18]。在未校正变量的情况下(Model 1),与低TG/HDL-C比值的患者相比,高TG/HDL-C比值的患者发生高危CRA的OR值是1.430(95%CI:1.187~1.723,P<0.001)。在校正年龄、性别、吸烟、饮酒史4个变量后(Model 2),高TG/HDL-C比值患者出现高危CRA的风险是低TG/HDL-C比值患者的1.235倍

表2 高危CRA的代谢相关危险因素的多因素分析

Tab 2 Multivariate analysis of metabolism-related risk factors for high-risk CRA

Variables	OR	95%CI	*P*
Age (y)			
<50	1.000		
≥50	1.784	1.361-2.338	**<0.001**
Gender			
Female	1.000		
Male	1.338	1.052- 1.703	**0.018**
Smoking			
No	1.000		
Yes	1.455	1.017-2.081	**0.040**
Drinking			
No	1.000		
Yes	1.836	1.213-2.780	**0.004**
Hypercholesterolemia			
No	1.000		
Yes	0.807	0.618-1.054	0.115
Low HDL-C			
No	1.000		
Yes	1.287	1.023-1.619	**0.031**
High ALT			
No	1.000		
Yes	0.740	0.481-1.138	0.170
High GGT			
No	1.000		
Yes	0.709	0.48-1.046	0.083
Hyperglycemia			
No	1.000		
Yes	1.101	0.853-1.421	0.460
NAFLD			
No	1.000		
Yes	1.481	1.137-1.930	**0.004**
Hypertension			
No	1.000		
Yes	1.327	1.048-1.680	**0.019**
CAD			
No	1.000		
Yes	1.624	0.950-2.774	0.076

OR：Odds ratio；HDL-C：High density lipoprotein cholesterol；ALT：Alanine aminotransferase；GGT：Gama-glutamyl transpeptidase；NAFLD：Non-alcoholic fatty liver disease；CAD：Coronary artery disease.

（校正OR=1.235，95%CI：1.011～1.510，*P*=0.039）。而在校正年龄、性别、吸烟、饮酒、HBP史、CAD、高血糖（Model 3）后，高TG/HDL-C比值患者出现高危CRA的风险较低TG/HDL-C比值患者增加了22.2%（校正OR=1.222，95%CI：0.999～1.495，*P*=0.051）。

NAFLD患者FIB-4指数与高危CRA的相关性 NAFLD的严重程度是CRA的危险因素[19]。FIB-4指数可用于定义NAFLD肝纤维化分级[16]，当FIB-4指数＞2.67时，认为NAFLD合并中-重度肝纤维化。表4显示了NAFLD患者FIB-4指数对高危CRA的影响。在未校正变量的情况下，高FIB-4指数（＞2.67）NAFLD患者发生高危CRA的风险是低FIB-4指数（≤2.67）NAFLD患者的1.849倍（OR=1.849，95%CI：0.354～9.667，*P*=0.466）。在校正年龄、性别、吸烟、饮酒、HBP、CAD、高血糖、高TC、低HDL-C、高ALT和高GGT变量后，高FIB-4指数NAFLD患者发生高危CRA的风险较低FIB-4指数NAFLD患者增加了43.5%（校正OR=1.435，95%CI：0.218～9.448，*P*=0.707）。

讨 论

CRC仍是全球范围内发病率和死亡率很高的恶性肿瘤之一。饮食结构（如红肉、大量油炸食品和含糖饮料和甜点的摄取[20]）、熬夜[21]、吸烟和饮酒[22-23]等不良生活方式能促进CRN的发生。性别对CRA发生的影响机制仍未完全明确。研究表明，男性患者发生CRA可能与男性患者对CRN危险因素（如吸烟、饮酒、进食更多肉类等）的更多暴露有关；而女性CRN的风险降低可能与雌激素受体的存在、胰岛素样生长因子的降低等有关[24-25]。随着生活方式的改变和饮食结构的调整，CRC的发病率似有下降趋势，但这种下降趋势往往多见于发达国家，这可能与结直肠镜筛查的推广和内镜下切除癌前病变密切相关[26]。既往研究发现，50岁以后腺瘤性息肉患病率急剧增加[27]，进展期CRA发生CRC的风险明显高于非腺瘤患者[28]。与进展期CRA（直径≥1 cm，高度异型增生，或存在绒毛状或管状绒毛状组织学）的定义[28]不同的是，2020年ESGE不再强调绒毛结构[4]，完全切除病灶的低危病变无需内镜监测，高危病变需3年内内镜下监测，这意味

着,高危腺瘤可能是内镜随访的重点。

代谢功能障碍被认为参与CRN的发生及发展[8,29-31]。本研究采用胰岛素抵抗的评估指标(TG/HDL-C比值)探讨其与高危CRA发生的相关性,结果显示,高TG/HDL-C比值者发生高危CRA的风险高于低TG/HDL-C比值者,这与来自我国北方的一项前瞻性研究发现TG/HDL-C比值升高增加成人CRC发病风险的结论一致[32]。在一项回顾性研究中,NAFLD组的CRA患病率明显高于对照组(40.7% *vs*. 28.1%),在调整了高脂血症、糖尿病和肥胖的多变量模型中,NAFLD仍是CRA的危险因素(OR=1.74; 95%CI: 1.05~2.88, P=0.032)[30]。NAFLD与CRA的高风险和数量密切相关,而与其位置和大小无关[33]。将NAFLD患者根据肝病严重程度的非侵入性参数进一步分层时,严重肝病患者发生CRN的风险高于轻度肝病患者[6,19]。在本研究中,高FIB-4指数的NAFLD患者发生高危CRA的OR值高于低FIB-4指数,但差异无统计学意义;因此,我们建议未来研究可考虑通过瞬时弹性成像技术检测肝脏脂肪衰减参数或进行肝穿刺,以评估NAFLD严重程度与高危CRA的相关性。来自我国台湾省的一项前瞻性研究发现,HBP是男性进展性CRA的危险因素[31],与我们的研究结果类似。尽管已有研究认为T2DM[7]及CAD[34]是CRA的危险因素,但在此次回顾性分析中,LASSO回归结果显示CAD和高血糖虽然被认为是高危CRA的危险因素,但多因素回归分析表明其存在与否并未显著影响高危CRA的风险。

有研究发现,高水平的HDL-C具有抗炎、抗氧化及胆固醇逆向转运功能[35],其中HDL颗粒还可以通过影响免疫应答来抑制CRC的发生[36]。HDL颗粒的数量和结构依赖于脂质转运蛋白卵磷脂:胆固醇酰基转移酶(lipid transfer proteins lecithin: cholesterol acyltransferase,LCAT)和胆固醇酯转运蛋白(cholesteryl ester transfer protein,CETP)的活性[37]。一项前瞻性研究发现,CRC患者CETP活性升高,LCAT活性降低,当CETP存在或LCAT缺乏将导致严重的低HDL-C和显著增高的氧化应激水平;这意味着HDL-C水平的改变以及HDL结构的改变可能在CRC病变中起作用[37]。一项荟萃分析结果显示,血清HDL-C水平升高与CRC的患病呈负相关[38]。我们的研究数据亦表明,与NC组相比,高危CRA组血清HDL-C显著降低,且低HDL-C水平是高危CRA的独立危险因素。

肝脏衍生的代谢产物(如谷氨酰胺、胆红素和胆汁酸)可能通过肠道菌群作用,导致了CRC的发生[39-41]。目前关于肝功能指标与CRC风险关系的直接证据仍然有限且不确定。一项来自英国的前瞻性队列研究纳入了375 693名参与者、中位随访时间是10年,随访期内记录了2 662例CRC病例,结果发现,正常范围内较高的ALT、AST和GGT的循环水平与CRC风险呈负相关[42]。还有研究提出,正常范围内较高的ALT水平具有抗炎作用[43]。我们的研究发现,与NC组相比,高危CRA组患者的ALT、AST、GGT及ALP的平均水平更低、但这两组人群的4种肝酶均在正常范围内;在进行多因素分析时,我们未能发现肝酶水平与高危CRA的发病风险之间存在显著关系。因此,我们认为需要更多的临床研究,尤其是前瞻性研究,以进一步验证肝功能指标与高危CRA风险之间的关系。

作为一项回顾性研究,本文存在以下局限性:(1)针对的是代谢相关的病史和理化指标,缺乏腰/臀围、体重、体质指数、生活方式(如红肉摄入、锻炼情况)、一级亲属CRN家族史、化学预防药物的使用(如阿司匹林)等其他文献报道的与CRC发病风险相关的变量[44],故难以全面评估CRA患病的所有危险因素。(2)有研究提出较高的乙醇摄入是CRN的危险因素[23,45],但我们此次仅对"饮酒的存在与否"进行定性分析,而未对纳入人群进行乙醇摄入量的进一步定量,故难以发现乙醇与CRA间的剂量-反应关系。(3)仅纳入肠镜检查人群,样本量也有限,可能代表性不够,需要更多病例或前瞻性研究进一步验证。

代谢因素与高危CRA之间存在显著关联。年长(≥50岁)、男性、吸烟史、饮酒史、低HDL-C血症、NAFLD和HBP病史是高危CRA的独立危险因素;此外,高TG/HDL-C比值(≥2.68)的患者发生高危CRA的风险显著增加。这意味着,代谢异常的老年男性可能是结直肠镜筛查的重点人群。

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