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## 结肠镜检查患者肠道准备健康教育模式的 累积 Meta 分析与试验序贯分析

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目的:运用累积 Meta 分析方法评价强化健康教育对结肠镜检查患者在肠道准备质量、依从性、息肉/腺瘤检出率与重复肠道准备意愿的干预效果。

方法:计算机检索中国知网、万方、中国生物医学文献数据库(EBM)、Web of Science、Pubmed、Cochrane Library、EMBASE 数据库,搜集强化健康教育对结肠镜检查患者肠道准备质量影响的随机对照试验,检索时限为建库至 2021 年 10 月。由 2 名研究者独立筛选文献、提取、核对资料并评价纳入研究的偏倚风险后,所有纳入文献按照 Cochrane 系统评价手册 5.1.0 质量标准进行评价并进行质量等级评定,采用 Stata16.0 软件对纳入研究按照样本量大小进行累积 Meta 分析,同时应用 TSA0.9 软件进行试验序贯分析方法,评价研究结果的可靠性与真实性。

结果:共纳入 21 篇文献,8111 例患者,其中 14 篇质量等级为 A 级,7 篇质量等级为 B 级。累积 Meta 分析结果显示,强化健康教育可改善结肠镜检查患者肠道准备质量[OR=2.25,95%CI(1.87, 2.72)]、依从性[OR=2.99,95%CI(2.17, 4.13)]、息肉检出率[OR=1.25,95%CI(1.09, 1.43)]、腺瘤检出率[OR=1.76,95%CI(1.28, 2.41)]和重复肠道准备意愿[OR=3.13,95%CI(2.07, 4.74)],P 值均<0.05,差异均有统计学意义。试验序贯分析结果显示,肠道准备质量与重复肠道准备意愿现有结果可能存在假阳性:肠道准备质量累积 Z 值跨过传统界值,但未达到试验序贯分析界值,且累积信息量未达到 RIS(53272 例);重复肠道准备意愿样本量累积 Z 值穿过传统界值,其累积信息量未达到 RIS(41463 例)。依从性累积 Z 值同时穿过传统 Z 值和 TSA 界值,表示虽然 RIS 未达到期望值(11262 例),但不需要更多试验,已提前得到确证效果;息肉/腺瘤检出率方面,当纳入第 2 个研究时,累积 Z 值穿过 TSA 界值,提示此时已可证实强化健康教育在结肠镜检查患者息肉检出率中效果优于常规教育,且随着后续研究的加入,进一步验证强化健康教育的有效性。

结论:强化健康教育可有效改善患者依从性与息肉/腺瘤检出率,肠道准备质量与重复肠道准备意愿仍需大样本、高质量的随机对照试验进一步验证效果。

## 南京地区心内科医师对阿司匹林副作用问卷调查

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目的:探讨了解心内科临床医师对于阿司匹林致消化道副作用认知水平。

方法:对南京市三级医院消化科、心内科临床医师进行阿司匹林致消化道副作用知识问卷调查。

结果:心内科医师 144 份,收回 142 份,心内科临床医师对于小剂量阿司匹林能否引起胃肠道反应(准确率为 44.4%);阿司匹林致溃疡高危因素(准确率为 46.5%),服用阿司匹林无胃肠反应者是否检测 HP 并根除(准确率为 35.4%),消化科医师 254 份,收回 251 份,相比消化科临床医师,准确率分别为 96.0%、89.7%、72.8%(P<0.05)认知了解很差。

结论:对于阿司匹林致消化道副作用知识的学习和宣传,需要进一步加大力度,以尽量避免副作用的发生。

## 机器学习集成模型对上消化道出血患者再出血风险的预测

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目的:本研究旨在利用机器学习构建上消化道出血患者再出血的预测模型,以协助临床医生早期识别高危人群并实施合理干预。

材料:本研究回顾性收集 2016 年 1 月 1 日至 2019 年 12 月 31 日于苏州大学附属第一医院就诊的上消化道出血患者的临床数据,包括一般情况、临床表现、实验室检查、内镜图片、病情转归等,构成数据集 D。

方法:首先,由两名资深的内镜专家对 D 数据集中的内镜图片进行 Forrest 分级(“人工评分系统”),再利用深度学习的卷积神经网络(CNN)框架训练这些带有标签的内镜图片,并建立分类器(Forrest 分级)。接着,将分类器的预测概率转换为分类变量(“机器评分系统”),联合 D 数据集的结构化数据,构成新的数据集 D1;利用 H2O 平台的自动化机器学习函数将其按 8:2 比例随机划分训练集 T1 和验证集 V1;先训练数据集 T1,建立集成模型 B,再在 V1 中进行验证,以保证模型 B 的性能。最后,比较模型 B 和“人工评分系统”对预测上消化道患者再出血风险的能力。模型评价指标包括敏感度、特异度以及接收者操作特征曲线(ROC)下面积(AUC),模型可解释性工具包括变量重要性排序、Shapley 分析图(SHAP)、部分依赖性图(PDP)以及局部可解析性算法(LIME)。

结果与结论:一共纳入 375 例患者,有 16 例患者发生了再出血事件。其中 66 例患者为女性,平均年龄为  $54.22 \pm 16.92$  岁;309 例患者为男性,平均年龄为  $54.13 \pm 16.90$  岁。一共采集 1400 张内镜图片,通过深度学习的 DenseNet121 算法构建分类器,并计算同一个患者对应的内镜图片的概率平均值,得到该患者的“机器评分系统”,作为分类变量纳入数据集 D。最终,经过自动化机器学习训练和验证,得到的最佳集成模型为基于 Deep learning 算法的模型(DL 模型)。该模型在训练集的 AUC 为 0.705,敏感度和特异度分别为 0.417 和 0.993;在验证集的 AUC 为 0.494。“人工评分系统”的 AUC 在训练集和验证集上分别为 0.675 和 0.525。采用 DeLong 比较“人工评分系统”和 DL 模型的 AUC,两者之间无统计学差异(训练集  $P=0.771$ ,验证集  $P=0.838$ )。此外,机器学习花费的时间显著低于人工(前者平均 40s,后者平均 16h45min)。就 DL 模型来说,变量重要性排序表明,“机器评分系统”、晕厥、呕血、血红蛋白和非甾体类抗炎药物服用史、便血为重要变量,权重均超过 0.85。因此,利用深度学习自动分类内镜图片,并将其嵌套入临床结构化数据,通过自动化机器学习构建集成模型,这种方法可以在一定程度上提升预测能力,而且快速高效,为临床工作减轻负担。

## 基于深度卷积神经网络的 Forrest 评分模型的构建

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目的:本研究旨在利用深度卷积神经网络,构建非静脉曲张性上消化道出血患者内镜图片的 Forrest 评分模型,以提高临床医生对消化道出血内镜图片诊断的准确性。

材料:本研究回顾性收集 2016 年 1 月 1 日至 2019 年 12 月 31 日于苏州大学附属第一医院就诊的非静脉曲张性上消化道出血患者的临床数据,包括一般情况(身高、体重、年龄、性别等)、临床表现(呕血、黑便、便血、晕厥等)、实验室检查(血红蛋白、肌酐、尿素、白蛋白等)、内镜图片、病情转归(好转、再出血、死亡等),构成数据集。

方法:首先,由两名资深的内镜专家(10 年以上的内镜操作经验)对数据集中的内镜图片进行 Forrest 分级,作为金标准。再利用深度学习的卷积神经网络(CNN)框架对这些带有标签的图片进行学习并构建分类器。将数据集以 8:2 比例随机分为训练集( $n=1120$ )和验证集( $n=280$ ),在训练集上学习并构建分类器,在验证集上评价其性能。接着,将图片抹去标签,由一位年轻医生(1 年以内的内镜操作经验)独立对这些图片进行 Forrest 分级。最后,将分类器的准确性与年轻医生的准确性进行比较。

结果与结论:一共纳入 375 例患者,其中 66 例患者为女性,平均年龄为  $54.22 \pm 16.92$  岁;309 例患者为男性,平均年龄为  $54.13 \pm 16.90$  岁。一共采集 1400 张内镜图片,通过深度学习的 DenseNet121 算法构建分类器,结果显示在验证集上准确性达 96.79%(271/280)。年轻医生对验证集的图片进行 Forrest 分级,准确性达 76.43%(214/280)。由此可见,基于深度卷积神经网络构建的 Forrest 评分模型的准确性明显高于年轻医生。因此,深度学习应用于内镜图片的分类能有效提高诊断准确性,具有一定的临床实用性。

## 早期食管癌内镜下治疗后食管狭窄的危险因素分析

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目的:食管癌作为我国最常见的恶性肿瘤之一,发病率高、预后差,严重威胁国民生命健康。随着消化内镜诊疗技术的发展,内镜下治疗凭借创伤小、恢复快等优点,已成为治疗食管早癌及癌前病变的主要方式。但内镜治疗术后引起的食管狭窄问题也需要引起重视,尤其环周型食管病变出现术后狭窄概率极高,治疗较为困难,部分患者出现顽固性食管狭窄,需反复球囊扩张,严重影响患者的生存质量并增加医疗费用,是临床上治疗的一个难点,但目前关于食管内镜术后狭窄概率的研究结果差异很大。本研究旨在探讨早期食管癌患者内镜治疗后发生食管狭窄的危险因素,并构建多因素内镜术后食管狭窄风险预测模型,实现早期预测及干预,为进一步降低食管早癌术后狭窄的发生提供理论依据。

方法:纳入 2017 年 1 月至 2022 年 5 月在东南大学附属中大医院接受内镜治疗的 200 例食管早癌及癌前病变患者,根据术后是否发生食管狭窄,分为狭窄组和非狭窄组,对两组患者纵向长径、环周范

围、浸润深度、有无脉管/神经侵犯、基底切缘是否阴性、分化程度等因素进行统计学分析,筛选术后发生食管狭窄的危险因素,并建立术后狭窄风险预测模型。随后运用该模型回顾性分析 50 名食管早癌内镜治疗患者,以检测灵敏度和特异性。

结果:两组患者基线指标无统计学差异( $P>0.05$ );单因素分析显示:狭窄组病变浸润深度、环周范围、纵向长径明显大于未狭窄组( $P<0.05$ ),术中食管肌层损伤比例明显高于未狭窄组( $P<0.05$ ),分化程度明显低于未狭窄组( $P<0.05$ ),且往往存在脉管浸润。位于颈部及胸上段的病变术后食管狭窄风险高于胸中、下端病变( $P<0.05$ )。有食管内镜手术史的患者术后狭窄风险高于无相关手术史的患者( $P<0.05$ )。多因素 logistic 回归分析显示两组间病变浸润深度、环周范围、纵向长径、病理类型、术中食管肌层损伤均为术后食管狭窄的危险因素( $P<0.05$ ),纳入以上多因素显著指标,建立预测模型,再次回顾性分析 50 名食管早癌内镜治疗患者,模型总准确率为 88%,灵敏度和特异性俱佳。

结论:本研究显示,病变浸润深度、环周范围、纵向长径、组织病理类型、术中食管肌层损伤、病变部位、既往食管内镜手术史是患者发生食管狭窄的高危因素,其中切除范围大于 3/4 环周和浸润深度超过 M2 为发生术后狭窄的独立危险因素。此研究为术后食管狭窄的发生提供了理论依据。目前尚无术后预防性治疗食管狭窄的明确标准,临床治疗中可根据此预防性使用球囊扩张、类固醇类激素及生物制剂,予患者早期临床干预,预防术后狭窄,提高患者生存质量。

## 一种新型封堵器治疗难治性上消化道气道瘘 的有效性及其安全性研究

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目的:目前上消化道气道瘘治疗棘手、总体疗效差,患者生活质量极低、病死率高。为此我们自主研发出一种新型消化道瘘封堵器,本临床研究旨在探究新型封堵器治疗难治性上消化道气道瘘的短期有效性及安全性。

方法:本临床研究为前瞻性、单中心、单臂设计。根据纳排标准入组难治性上消化道气道瘘患者行新型封堵器置入术,记录患者术前一般资料、手术及住院资料,术后 1、3 月随访并复查胃镜、支气管镜及靛胭脂试验,主要有效性终点为术后 1、3 月有效封堵率,次要有效性终点为技术成功率、术后 1、3 月完全封堵率、术后 3 月 BMI、SF-36 生活质量评分较基线的变化。安全性终点为出血、发热、疼痛、移位脱落等不良事件发生率。

结果:2020 年 9 月至 2021 年 11 月期间在南京医科大学第一附属医院消化内科共纳入 23 例患者接受新型封堵器置入术,其中 19 例男性、4 例女性,平均年龄  $63.1 \pm 6.1$  岁,平均 BMI 为  $17.3 \pm 2.4 \text{ kg/m}^2$ ,19 例(82.6%)病因为外科手术和(或)放疗,瘘中位病程 5 月(3~129 月),瘘中位直径 6mm(3~19mm),11 例(47.8%)为胸腔胃瘘,8 例(34.8%)为食管瘘,4 例(17.4%)为食管-胃吻合口瘘。15 例(65.2%)患者接受了腔内型封堵器置入术,8 例(34.8%)接受了腔外型封堵器置入术,两组平均手术时间分别为  $25.1 \pm 5.3 \text{ min}$ 、 $30.8 \pm 11.3 \text{ min}$ ,无显著统计学差异,技术成功率 100%,术中均无出血、穿孔等并发症,平均术后住院时间为  $3.4 \pm 1.5$  天,出院时鼻肠管拔除率为 100%(20/20),恢复经口进食率 100%(23/23)。术后 1 月评估有效封堵率为 91.3%(21/23),其中完全封堵率 60.9%(14/23),近全封堵率 30.5%(7/23),2 例(8.7%)患者为无效封堵,予行封堵器置入术。术后 3 月有效封堵率为 95.7%(22/23),其中完全封堵 52.2%(12/23),近全封堵率 43.5%(10/23),仅 1 例(4.3%)患者为无效封堵。术后 3 月患者平均 BMI 和 SF-36 生活质量评分较基线均显著升高( $p$

$<0.001$ ;  $p<0.01$ ),提示封堵术后患者营养状况及生活质量显著提高。此外,2例患者在更长的随访中出现了单侧甚至双侧瘘口愈合,提示原机械性封堵的治疗目标有望提升为生物性愈合。9例(39.1%)患者共出现14例不良事件,但多为轻微或一过性症状,且无手术或器械相关性死亡。

结论:临床应用该新型封堵器治疗难治性上消化道气道瘘短期内是有效及安全的,这为消化道瘘的内镜治疗提供了一种新器械、新术式,有望成为该类患者的挽救治疗方案。

## 基于自动机器学习算法的 ERCP 术后胆总管结石复发预测模型

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目的:本研究旨在利用自动机器学习算法,构建患者 ERCP 术后胆总管结石复发的预测模型,以提高临床医师对结石复发预测的准确性

材料:本研究回顾性收集 2013 年 1 月 1 日至 2018 年 12 月 30 日,于苏州大学附属第一医院进行 ERCP 手术的 473 名患者数据。数据包括患者的一般情况(BMI,年龄,性别等);实验室检查(钾离子,钙离子等);ERCP 手术操作方式(球囊扩张,机械碎石等);结石性质(结石大小,数量)。

方法:实验数据按照 7:3 比例,随机分为训练集与验证集。为更好探究自动机器学习相较传统 Logistic 回归,于临床预测模型方面的表现,本研究采用三种不同的算法建立 ERCP 术后预测模型:全自动机器学习(即 ERCP 相关危险因素未经临床医师人工筛选,直接载入 H2O 自动机器学习平台,由自动机器学习算法完成模型的构建以及危险因素的识别);半自动机器学习(即 ERCP 相关危险因素经由临床医师手动初步识别后,载入 H2O 自动机器学习平台,由自动机器学习算法完成模型的构建以及对危险因素的进一步识别);传统 Logistic 回归(即已在临床上广泛运用的建立预测模型方式,经由单因素 Logistic 回归,多因素 Logistic 回归后,建立临床预测模型)。训练集数据运用上述算法分别建立预测模型,并于验证集数据进行模型性能评价。同时,依靠自动机器学习良好的模型可视觉解释能力,我们对预测模型进行了详细的可视觉解释。

结果:利用三种不同的算法,我们建立了三种 ERCP 术后结石复发的预测模型。其中,基于半自动机器学习算法的 GBM 模型,拥有最佳的曲线下面积(0.749),被认为是最佳模型,优于全自动机器学习模型(曲线下面积为 0.736)与 Logistic 模型(曲线下面积为 0.730)。同时,通过 SHAP 图,Local SHAP 图,部份依赖图,我们可视觉解释最佳模型中,各个变量(胆总管直径,结石数量,胆囊切除术史,结石直径)对结石复发的影响程度。

结论:利用自动机器学习,我们建立了预测 ERCP 术后胆总管结石复发的高性能模型,并利用可视化技术,对各个危险因素进行了详细解释。自动机器学习相较传统 Logistic 回归建模,其拥有更优异的性能以及模型的可解释性,值得临床推广运用。

# Development of Automated Machine Learning Models Using H2O Platform Based on Clinical Structured Data in Predicting Colorectal Adenoma in Non—alcoholic Fatty Liver Disease

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This research is to build an automated machine learning (AutoML) model using a structured data set to predict colorectal adenoma outcomes in 506 patients with NAFLD. The method included a logistic regression model and four AutoML models including Gradient Boosting Machines (GBMs), Generalized Linear Models (GLMs), Extremely Random Forest (XRF), and Deep Learning (DLs) algorithms. GBM had the best predictive ability which revealed the accuracy (0.735), PPV (0.729), NPV (0.741), sensitivity (0.754), specificity (0.714), and AUROC (0.791). In the GBM model, albumin showed the leading feature of all variables, followed by RBCs, AST—ALT ratio, PLT, and age in the occurrence of colorectal adenoma in intestinal extrahepatic complications.

## Risk factors and correlation of colorectal polyps with type 2 diabetes mellitus

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**Background:** Colorectal polyp is a common disease of the gastrointestinal tract, which is closely related to colorectal cancer. Diabetes mellitus (DM) is a major public health disease that seriously threatens human health. This study aimed to investigate the risk factors of colorectal polyps and its relationship with type 2 DM (T2DM).

**Methods:** A total of 352 patients with colorectal polyps (diagnosed by colonoscopy) in our hospital from June 2018 to June 2020 were enrolled as the observation group, and 201 healthy people with normal colonoscopy results were selected as the control group. The levels of blood lipids, blood glucose, liver function, serum uric acid (UA), and glycosylated hemoglobin (HbA1c) were compared between the two groups. Univariate and multiple logistic regression analyses were performed to analyze the risk factors related to colorectal polyps.

**Results:** Compared to the control group, the levels of HbA1c, fasting plasma glucose (FPG), 2—hour post—meal blood glucose (2hPG), total cholesterol (TC), and serum UA in the observation group were significantly higher ( $P < 0.05$ ). Univariate analysis showed that the incidence of colorectal polyps was significantly correlated with gender, smoking, age, non—alcoholic fatty liver disease (NAFLD), and type 2 diabetes mellitus (T2DM) ( $P < 0.05$ ). Multiple Logistic regres-



sion analysis showed that gender (male), age ( $\geq 60$  years), and T2DM were independent risk factors for colorectal polyps ( $P < 0.05$ ).

Conclusions: Abnormal metabolic indices may be closely related to the development of colorectal polyps. Gender (male), age ( $\geq 60$  years), smoking, NAFLD, T2DM, as well as increased blood glucose, UA, and TC were identified as the risk factors for colorectal polyps.

## Establishment of a model for predicting delayed postpolypectomy bleeding: a realworld retrospective study

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Background and Aim : Delayed postpolypectomy bleeding (DPPB) is the most common complication after endoscopic colorectal polypectomy, which occurs within 30 days after the surgery. This study aimed to investigate the probable predictors of DPPB and establish an accurate nomogram to predict its occurrence. Methods : This was a real-world case-control study based on medical records from The First Affiliated Hospital of Nanjing Medical University. Cases of patients who underwent colonoscopic polypectomy between January 2016 and December 2020 were reviewed to analyze the risk factors of hemorrhage after the surgery. Logistic regression analyses were performed to identify the independent risk factors. According to the results, we developed a predicted nomogram and evaluate its prediction efficiency. Results : A total of 16925 patients were performed colonoscopic polypectomy during this period, hemorrhage occurred in 125 (0.74%) cases, and 375 patients were enrolled in the control group. In the logistic regression analyses, the independent risk factors of DPPB included age (OR = 0.966), sex (OR = 3.282), hypertension (OR = 1.877), polyp location (OR = 2.125), polyp size (OR = 4.174), and operative modality (OR = 2.601). A nomogram was constructed based on these factors. The Cindex of the model is 0.801 (95% CI : 0.761 ~ 0.846). Conclusions : The nomogram has good performance in predicting the occurrence of DPPB, it can be used as a convenient screening tool to select patients with high risk of bleeding, in this way, physicians can enhance individual monitoring and make clinical decisions more accurately.

## EUS-FNA 诊断肺腺癌一例

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超声内镜是临床中胆胰系统疾病诊治的重要手段之一,通过超声内镜引导下的细针穿刺活检(EUS-FNA)可以获得消化道管壁外病灶的组织学标本,近年来超声内镜在非消化道疾病诊治中也发挥了一定的作用,但在肺内肿瘤性病变诊断中的作用罕有报道。本文报道了一例老年女性经EUS-FNA确诊为肺腺癌的病例,进一步探讨了超声内镜及EUS-FNA在肺内肿瘤性病变诊治中的

作用。

## 超声内镜诊断罕见胰管囊肿一例(含视频)

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胰管囊肿为腹胰管、背胰管局限性扩张,分两型:Wirsung 管末端局限性扩张(Wirsungocele)及 Santorini 末端局限性扩张(Santorinicele)。根据既往大部分文献报道,Wirsungocele 的主要发现手段为 MRCP 及 ERCP,本文报道一例老年男性患者在超声内镜下确诊 Wirsungocele,并通过此病例分享本中心于超声内镜下探查胰管变异的经验和心得。

## EUS-FNA 确诊肝脏和肾上腺双原发转移一例

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双原发恶性肿瘤少见,而在此基础上的不同器官的各自转移更是罕见。我们报道了首例肺、结肠同步恶性肿瘤经超声内镜引导下细针抽吸活检(endoscopic ultrasonography guided fine-needle aspiration, EUS-FNA)确诊肾上腺、肝脏不同来源转移的病例。

## 3 例少见的结直肠 ESD 术后迟发性出血治疗体会

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背景:内镜粘膜下剥离术(Endoscopic submucosal dissection, ESD)已经被广泛应用于结直肠病变的治疗。然而如何有效控制术后迟发性出血仍是亟待解决的问题。本文描述了 3 例少见的术后迟发性出血的病因及治疗方法。

方法:第一例为直肠神经内分泌肿瘤患者,既往有血友病 A,术前凝血因子Ⅷ(clotting factor Ⅷ, FⅧ)水平为 4%。目前尚无针对血友病患者接受 ESD 治疗的围术期管理标准。因此术前参照既往外科手术和 ERCP 治疗的经验,予 FⅧ 输注,提高 FⅧ 水平至 20%,直至术后第 1 天。ESD 术程顺利,术中予荷包缝合关闭创面。患者于术后第 5 天出院。患者于术后第 15 天出现便血,急查 FⅧ 水平仅为 2%,急诊肠镜示术区出血,荷包缝合在位,覆有新鲜血凝块,后经 FⅧ 输注治疗后好转。

第二例为乙状结肠早癌患者,既往有前列腺增生。ESD 术程顺利,术后第 3 天出院。患者于术后第 9 天出现少尿和便血,出血量约 800ml,化验结果示血肌酐(Scr)为 1449 $\mu$ mol/L,部分活化凝血酶原时间(APTT)为 74.8s,诊断考虑肾后性梗阻所致急性肾功能损伤及血凝障碍,予留置导尿管、输血、补液支持治疗后好转。

第三例为乙状结肠癌术后、直肠广基息肉患者。ESD 术中剥离粘膜后可见曲张的痔静脉,予钛夹

夹闭创面预防出血。术后第 12 天,患者出现严重的便血和失血性休克,急诊肠镜示术区的痔静脉破裂出血,遂立即予热活检钳和钛夹止血。追问病史,患者术后有用力排便史。

结果:此三例患者经上述诊疗后,出血均得到有效控制并痊愈出院。

结论:血友病 A 患者接受结直肠 ESD 治疗时,需在围术期输注 FⅧ,维持其水平 $\geq 20\%$ 至术后第 1 天,并需在术后继续监测,必要时再次输注以预防术后迟发性出血。对合并前列腺增生的患者,围术期需要充分调整好前列腺功能,避免出现肾后性梗阻及其所致的凝血功能异常,以预防术后迟发性出血。对于有痔静脉曲张或痔疮患者,在直肠 ESD 术后应设法保持排便顺畅,避免粪便干结和用力排便以致痔静脉破裂出血。结直肠 ESD 围术期的科学管理对预防术后迟发性出血有重要意义。

## Endoscopic submucosal dissection of coexisting early esophageal carcinoma and leiomyoma: a case report and review of the literature

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### Introduction

Esophageal squamous cell carcinoma (SCC) and esophageal submucosal tumor (SMT) are distinct neoplasms originating from different cell layers. Although simultaneous development of such carcinomas in the same esophagus are common, early esophageal cancer located within an area of submucosal tumor is relatively rare. In the case report below, we encountered a patient with acid reflux, heart burn and dysphagia, which was eventually diagnosed as early esophageal carcinoma combined with leiomyoma. After endoscopic submucosal dissection, the patient's clinical symptoms were relieved.

### Case report

A 78-year-old man presenting with acid reflux and heart burn of six months, dysphagia of two weeks duration after meals was recruited at the inpatient service of Department of Gastroenterology, the First People's Hospital of Changzhou. Before this, he did not complain of any melena, weight loss, fever or joint pain. Past history included hypertensive disease of ten years. Upon admission, a physical examination was unremarkable. In addition, as listed in Table 1, laboratory evaluation, including coagulation function, liver function, and serum tumor markers, were normal. A contrast enhanced thoracic computed tomography (CT) scan showed thickening of the esophageal wall at the right side of the upper third part of the thoracic esophagus. Endoscopy revealed a protruding lesion with a light reddish surface of  $0.3 \times 0.3$  cm within a shallow depressed area in the proximal third of the esophagus. The margin of the light reddish area showed disappearance of the vascular network in the mucosa. Endoscopic biopsy revealed highly differentiated squamous cell carcinoma (SCC). Endoscopic ultrasonography (EUS) demonstrated a hypoechoic tumor, 11 mm in diameter, confined to the submucosa with a well-demarcated and smooth outline, with the muscularis propria layer intact. Moreover, EUS demonstrated that the SCC overlaid one of the leiomyomas, originating in the muscular layer, suggesting that the cancer may have invaded only as far as the mucosa layer.

A tentative diagnosis was made of esophageal cancer, superficial type, IIc based on the Guidelines for Clinical and Pathologic Studies of Carcinoma of the Esophagus from the Japanese Society for Esophageal Disease. After obtaining informed consent, endoscopic submucosal dissection was carried out by aspiration lumpectomy. The resected specimen, measuring 35×33mm, consisted of two independent histological types of neoplasms. One was a leiomyoma that originated from the muscularis mucosa. Histopathological examination revealed low overall cellularity, and were composed of interlaced smooth-muscle cells with hypovascularity and no mitosis. Immunohistochemically, the tumor cells was positive for SMA (+), but were negative for CD117 (-) and CD34 (-). The other was a highly differentiated esophageal squamous cell carcinoma confined to the mucosa over the leiomyoma. The resected specimen showed M2 (Lamina propria) esophageal cancers with negative lateral margins. In addition, there was no evidence of lymphovascular invasion. His clinical symptoms improved significantly within 2 months. Repeated endoscopy at six months showed no evidence of recurrence.

#### Conclusion

To our knowledge, this is an unusual presentation of esophageal SCC located within an area of leiomyoma in the upper third of the esophagus, which emphasized the importance of accurate diagnosis of the depth of invasion using EUS. In addition, a non-invasive endoscopic therapeutic procedure should be chosen for those cases where a coexisting superficial carcinoma overlies a leiomyoma.

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## **A case report of endoscopic resection for the treatment of duodenal Brunner's Gland Adenoma with Upper Gastrointestinal Bleeding**

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#### Introduction

Brunner's gland adenoma (BGA), also named as polypoid hamartoma and Brunneroma, is an extremely rare benign duodenal tumour arising from the Brunner's gland of the duodenum. They were first described as a benign hamartomatous lesion characterized by the proliferation of Brunner's glands in 1835 by an American anatomist, Cruveilhier. Generally, they are asymptomatic and discovered by chance during upper gastrointestinal endoscopy or on an upper gastrointestinal series, as they are rarely larger than 2 cm. Occasionally, some present with chronic abdominal pain, nausea, vomiting, and anemia when they may be larger than 5 cm, and located in the duodenum. When they reach giant dimensions, they may obstruct the gastric outlet or duodenum, which requires surgery or endoscopic resection. Although a few case reports have previously described BGA patients with gastrointestinal bleedings, there are no systematic reports on the clinical features and treatments. In this case report, we retrospectively presented a rare patient with a duodenal polypoid mass of more than 7cm who was admitted to our department with upper gastrointes-

tinal bleeding and on which endoscopic mucosal resection was performed. Furthermore, we also systematically reviewed the patient's clinical presentation, imaging features, endoscopic picture, and possible treatment.

#### Case presentation

A 81-year-old female patient experienced with the chief complaints of melena for one weeks, accompanied by a progressive epigastric pain, weakness and fatigue, was recruited at the inpatient service of Department of Gastroenterology, the First People's Hospital of Changzhou. She had a past medical history significant for coronary artery disease and chronic atrial fibrillation for more than ten years subsided by anticoagulants. She had chronic episodic upper central abdominal pain for many years subsided by antisecretory medications; however, no history of melena previously. Presently, she denied any recent use of non-steroidal anti-inflammatory drugs (NSAIDs). Upon admission, her vital signs were quite unstable; heart rate was 80 beats/min, blood pressure was 102/70 mmHg; and respiratory rate was 20 breaths/min. Physical examination revealed an anemic man in weakened condition. Hematological evaluation revealed severe anemia with a hemoglobin level of 66 g/L. In addition, as listed in Table 1, other laboratory data, including coagulation function, liver function, and serum tumor markers, all within normal limits. The patient received a total of 2 transfusions of erythrocyte concentrates, after which the hemoglobin level remained stable at 80g/L. The chest and abdomen CT showed a large (4.5×5.5 cm diameter) hypervascular exophytic mass, which appeared to originate from the descending duodenum. Furthermore, there were no signs of invasion or dissemination. The emergency upper gastrointestinal endoscopy (EGD) revealed a large pedunculated mass located on the posterior surface of duodenal bulb with stigmata of recent hemorrhage. Endoscopic ultrasonography (EUS) revealed a submucosal polypoid mass, which was not possible to see the entirety of the mass due to its large size and moving stem. There was no evidence of *Helicobacter pylori*-associated gastritis. Furthermore, biopsies were not conclusive as the mass showed a quick inclination to bleed during biopsies. After multidisciplinary discussions, this mass lesion was considered to be most likely to be BGA, followed by gastrointestinal stromal cell tumor (GIST). Given the patient's advanced age, heart disease and the risk of bleeding at any time, endoscopic resection was planned. After the patient signed the consent, this mass lesion (6×7 cm diameter) was successfully totally removed by endoscopic submucosal dissection (ESD) for more than three hours. The postoperative period was uneventful and the pathologic diagnosis was assessed as Brunner's gland adenoma. Her tarry stools stopped after endoscopic therapy, and her hemoglobin levels improved to 90g/L after multiple blood transfusions. The follow-up EGD after 6 months showed white scar change on the posterior surface of the duodenal bulb.

#### Conclusion

We reported a extremely rare case of BGA patient with gastrointestinal bleeding as the main clinical manifestation. The lesion was diagnosed by radiologic imaging and endoscopic examination. ESD could be a safe and low-risk treatment for elderly patients with severe underlying diseases. However, because our observation is limited to 1 patient, more patients and longer follow-up are necessary.

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## 假肿瘤性胰腺炎 EUS 声像学特点分析

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目的:探讨假肿瘤性胰腺炎 EUS 下的声像学特点。

方法:回顾性分析苏州大学附属第二医院 2019 年 4 月—2021 年 9 月经外科手术或 EUS-FNA 病理诊断及随访结果确诊为假肿瘤性胰腺炎的患者资料,分析临床数据、EUS 下的声像特征、评估技术的成功率及 EUS-FNA 的准确性,判断 EUS 在该病中的诊断价值。排除标准:患者有凝血功能异常(血小板计数 $<60\times 10^9/L$ 或国际标准化比值 $INR>1.5$ );严重心肺疾病;无法耐受麻醉;不合作。

结果:共纳入 8 例患者,所有病例在治疗前均行 EUS 探查,其中 3 例行 EUS-FNA,术后病理提示慢性炎,未见肿瘤细胞;2 例行胰十二指肠手术治疗,其中 1 例治愈,1 例死亡,术后病理均提示胰腺慢性炎症。除手术切除病例,剩余 6 例均行抗炎治疗,随访过程中,行 EUS、CT 或 MRI 复查后病灶均有不同程度缩小或消失。8 例患者中 4 例(50%)合并有糖尿病,2 例患者(25%)合并有胆道疾病,2 例患者(25%)既往曾有过急性胰腺炎发作,3 例患者(37.5%)CA199 升高,2 例患者(25%)显示胆管扩张,8 例患者均无胰管扩张。

结论:通过反复对比假肿瘤性胰腺炎及胰腺癌的 EUS 声像特征,本研究总结发现假肿瘤性胰腺炎 EUS 表现具有以下特点:1. 大病灶常位于胰头部,与胆管关系密切,与胰管关系甚远,EUS 下呈现出低(外围炎症渗出)—高(中间出血坏死)—低(内部液化)类似于“黑洞”样的声像特征;而小病灶好发于胰体尾,与胆管关系甚远,与胰管关系较密切,EUS 下边界清晰,但回声不均匀,可见点状高回声,无蟹足样改变,最具特征的表现是胰管穿行于病灶内部,无远侧胰管的显著扩张表现;2. 血流信号:假肿瘤性胰腺炎往往病灶内部及周围血流信号丰富,血流信号与病灶大小呈正比,大病灶甚至会出现“花篮样”的血流特征;3. 周边淋巴结:假肿瘤型胰腺炎周边也会出现较多肿大淋巴结,但均为典型的炎性淋巴结声像(蚕豆样、回声偏高、淋巴门清晰可见)。超声内镜声在假肿瘤性胰腺炎中具有特征性的声像学改变,结合典型的 EUS 图像及临床资料,可为假肿瘤性胰腺炎诊治提供依据。

## 计算机辅助诊断技术对胃肠道间质瘤和平滑肌瘤 EUS 图像的鉴别诊断价值

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2. 上海市第十人民医院
3. 苏州大学计算机技术学院

目的:内镜超声(endoscopic ultrasonography, EUS)可以通过病变的起源层次、内部回声等特征对胃肠道上皮病变进行鉴别诊断。但胃肠道间质瘤和平滑肌瘤在 EUS 图像上均表现为低回声病灶,且两者起源层次相近,EUS 特点相似;因此仅凭 EUS 很难将两者区分。然而胃肠道间质瘤具有恶性潜能,需手术治疗;平滑肌瘤为良性病变,可以定期随访。因此,对两者进行鉴别诊断对后续治疗方案的制定以及预后的判断至关重要。基于深度学习的计算机辅助诊断技术可以获取 EUS 图像的像

素分布和空间变化等信息,以此建立分类模型对疾病进行鉴别,为内镜医生的诊断提供客观证据。本研究初步探索了基于 Resnet 网络结构的计算机辅助诊断技术在胃肠道间质瘤和平滑肌瘤的 EUS 图像鉴别诊断中的应用价值。

方法:纳入自 2014 年 10 月至 2021 年 10 月在苏州大学附属第二医院接受 EUS 检查、且行外科手术或内镜下手术治疗、经病理确诊的 69 例胃肠道间质瘤和 73 例平滑肌瘤患者。每个病例选取一张清晰且有典型病变的 EUS 图片,共计 142 张 EUS 图像。将选取的 142 张 EUS 图像按 8:2 的比例随机划到训练集和验证集中,113 张 EUS 图像(其中 55 张胃肠道间质瘤图像,58 张平滑肌瘤图像)组成训练集,通过旋转、翻转、对局部图像块采用标准化的直方图进行自适应均衡化、通过 log、sigmoid 相关公式改变像素点的值来改变对比度等对训练集中的图片进行扩增,利用扩增后的训练集对 Resnet 网络结构进行训练与优化,构建分类模型;比较基于 Resnet 34 和 Resnet 50 网络结构的分类模型的性能。最后利用验证集中的 29 张 EUS 图片(14 张胃肠道间质瘤图像、15 张平滑肌瘤图像)对分类模型进行验证,评估 Resnet 网络结构对胃肠道间质瘤和平滑肌瘤的鉴别诊断价值。

结果:将训练集中的数据扩大 6 倍后,得到 678 张 EUS 图像(其中 330 张胃肠道间质瘤图像,348 张平滑肌瘤图像);利用 Resnet 34 网络结构建立的分类模型对胃肠道间质瘤和平滑肌瘤进行鉴别诊断的准确率为 88.8%,较 Resnet 50 网络结构(81.4%)的分类性能更佳。基于 Resnet 34 网络结构的分类模型对验证集中的 EUS 图像进行分类诊断的灵敏度、特异度、阳性预测值、阴性预测值、准确率分别为:85.71%、93.33%、92.31%、87.5%、89.66%。

结论:基于 Resnet 34 网络结构的计算机辅助诊断技术对胃肠道间质瘤和平滑肌瘤进行鉴别诊断是可行的,且具有客观、快速、无创等优点,可以为临床医生对两者的鉴别提供辅助诊断意见。

## 支持向量机对胃肠道间质瘤和平滑肌瘤 EUS 图像的鉴别诊断价值

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目的:胃肠道间质瘤和平滑肌瘤在 EUS 图像上均表现为低回声病灶,两者起源层次相近,EUS 特点相似;因此仅凭 EUS 很难将两者区分开来。然而,胃肠道间质瘤具有恶性潜能,需要手术治疗,平滑肌瘤为良性病变,可以定期随访,对两者进行鉴别诊断对后续治疗方案的制定以及预后的判断至关重要。机器学习通过算法从图像数据中提取和选择特征,将获得的特征作为输入值,建立分类模型对新的样本数据进行预测和判断。支持向量机是机器学习中一种非常强大的二分类模型。因此,本研究中,我们探索了支持向量机在胃肠道间质瘤和平滑肌瘤的 EUS 图像鉴别诊断中的应用价值。

方法:纳入自 2014 年 10 月至 2021 年 10 月在苏州大学附属第二医院接受 EUS 检查、且行外科手术或内镜下手术治疗、经病理确诊的 69 例胃肠道间质瘤以及 73 例平滑肌瘤患者。每个病例选取一张清晰且有典型病变的 EUS 图片,共计 142 张 EUS 图像。勾画每张 EUS 图像的感兴趣区域,在感兴趣区域内截取最大的矩形子图组成数据集。使用 Matlab 软件对矩形子图进行分析,提取纹理特征;采用 ReliefF 权重法联合顺序前进法对纹理特征进行筛选,获取最佳的纹理特征组合;随后基于支持向量机建立分类模型,采用对半法对数据集进行划分,对分类模型进行训练优化并验证其分类性能。

结果:初始提取到 17 大类 105 维纹理特征,经过特征筛选后,得到 2 大类 10 维特征作为最佳纹理

特征组合。利用支持向量机建立分类模型,该模型对胃肠道间质瘤和平滑肌瘤进行鉴别诊断的灵敏度、特异度、阳性预测值、阴性预测值、准确率分别为:77.14%、91.67%、80.49%、90.00%、84.51%。

结论:基于支持向量机建立的分类模型具有较高的诊断特异度,对胃肠道间质瘤和平滑肌瘤进行鉴别诊断是可行的,且具有无创、客观等优点,可以为临床医生对两者的鉴别提供辅助诊断意见。

## 标准化健康教育对消化内科幽门螺杆菌阳性患者疾病认知及服药依从性的影响

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标准化健康教育对消化内科幽门螺杆菌阳性患者疾病认知及服药依从性的影响曹琳琳,顾婷徐州市第一人民医院 消化内镜中心 江苏徐州 221100 通讯作者:陈光侠课题名称:幽门螺杆菌感染个体化治疗及胃癌综合防治体系的构建(BE201964)摘要:目的:分析探索标准化健康教育对消化内科幽门螺杆菌(Hp)阳性患者疾病认知及服药依从性的影响。

方法:收集 2020 年 1 月~2020 年 10 月于我院消化内镜中心就诊的 Hp 阳性患者 72 例,根据随机原则分为实验组(n=36)与对照组(n=36),对照组患者接受常规随访干预,实验组患者在此基础上接受标准化健康教育,比较两组患者的疾病认知度及服药依从性。

结果:实验组患者干预后的疾病认知评分显著高于对照组( $P<0.05$ );实验组患者干预后的服药依从评分显著高于对照组,K10 量表评分显著低于对照组( $P<0.05$ );实验组患者干预后的健康自我管理评分显著高于对照组( $P<0.05$ )。实验组患者的 Hp 感染根治率显著高于对照组( $P<0.05$ )。

结论:标准化健康教育可提高 Hp 阳性患者的疾病认知度,减轻患者的心理困扰程度,提高患者的服药依从性,改善患者的健康自我管理行为。研究结果表明,实验组患者干预后的疾病认知评分显著高于对照组( $P<0.05$ );提示标准化健康教育能够为患者详细提供疾病相关专业知识,从而增加患者对疾病的了解程度。表 2 中,实验组患者干预后的服药依从评分显著高于对照组,K10 量表评分显著低于对照组( $P<0.05$ );提示标准化健康教育能够减轻患者的心理困扰,帮助患者积极配合治疗,从而增强患者的服药依从。表 3 中,实验组患者干预后的健康自我管理评分显著高于对照组( $P<0.05$ );提示标准化健康教育能够有效提高患者的自我管理能力,改善其自我管理行为。本研究结果发现,实验组患者的 Hp 感染根治率显著高于对照组( $P<0.05$ );提示实施标准化健康教育后患者对 Hp 感染的认知度提高,意识到遵医嘱服药对病情控制的重要性,有效提高患者的服药依从性,且明显改善患者的健康自我管理行为,避免各种外源性因素影响而加重病情,有效提高治疗效果,进而增加 Hp 感染根治率。综上所述,标准化健康教育可提高 Hp 阳性患者的疾病认知度,减轻患者的心理困扰程度,提高患者的服药依从性,改善患者的健康自我管理行为。

## 抗 VEGF-A 探针在示踪胃癌及癌前病变中的应用研究

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目的:探究基于血管内皮生长因子 A(VEGF-A)的单克隆抗体——贝伐单抗的荧光探针在示踪



胃癌及癌前病变中的应用价值。

方法:搜索 TCGA 数据库中 VEGFA 在胃癌及癌旁组织中的表达。选择无锡市人民医院外科及内镜术后的胃癌和胃癌前病变病理标本,用免疫组化的方法比较 VEGFA 在病变及邻近组织中的表达。合成荧光标记的贝伐单抗探针,并在胃癌细胞系及人胃黏膜上皮细胞系中验证探针的亲合力。构建胃癌皮下瘤小鼠模型,利用活体荧光成像探索贝伐单抗探针示踪肿瘤区域的作用。在内镜黏膜剥离术后新鲜的病变组织表面喷洒贝伐单抗探针,在荧光内镜下评估该探针用于区分正常胃黏膜与病变组织的应用价值。

结果:TCGA 数据显示,与正常组织中的水平相比,胃腺癌组织中的 VEGFA 表达明显高于癌旁组织( $P < 0.05$ )。免疫组化结果表明,与邻近组织相比,VEGFA 在胃癌组织和胃异型增生组织中的表达均更高( $P < 0.05$ )。贝伐单抗探针与胃癌细胞系的亲合力优于人胃黏膜上皮细胞系( $P < 0.05$ )。活体荧光成像说明,贝伐单抗探针可以在胃癌皮下瘤小鼠中特异地示踪胃癌区域。利用荧光内镜可以在喷洒贝伐单抗探针后的 ESD 术后标本中观察到,胃早癌及癌前病变区域的荧光强度明显高于正常的胃黏膜组织。

结论:近红外抗 VEGFA 探针是一种潜在的筛查胃癌及癌前病变的新型途径。

## 生命帮助计划多学科协作对内镜低血糖的影响

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目的:分析以生命帮助计划为基础多学科协作对糖尿病患者内镜检查术围术期低血糖的防控效果。

方法:选取 2018 年 6 月—2020 年 6 月期间我院收治的 118 例糖尿病患者内镜检查术为研究对象,随机数字表法分为观察组( $n=59$ )和对照组( $n=59$ ),分别给予以生命帮助计划为基础多学科协作的综合干预和常规围术期护理。比较干预前(T0)、内镜检查前(T1)、内镜检查后(T2)、干预 3d(T3)、干预 7d(T4)、干预 14d(T5)两组的血糖、血红蛋白水平和低血糖发生情况,并比较两组干预前、后的生活质量和对内镜检查术的满意度。

结果:T0—T2 两组的血糖、血红蛋白水平比较无明显差异( $p > 0.05$ ),T0—T2 两组均未发生低血糖( $p > 0.05$ ),T3—T5 两组的血糖、血红蛋白水平较 T0 均降低,且 T3 和 T4 时观察组的血糖、血红蛋白水平均高于对照组,对照组 T3—T5 内血糖、血红蛋白水平逐渐升高;T3—T5 时观察组的低血糖发生率分别为 1.69%、3.39%、3.39%,均低于对照组,差异有统计学意义( $p < 0.05$ )。T5 时两组的生活质量各项指标评分均高于 T0,且观察组高于对照组;观察组和对照组对内镜检查术满意度分别为 94.92%和 72.88%,差异有统计学意义( $p < 0.05$ )。

结论:通过以 HELP 为基础的多学科综合干预后观察组患者的低血糖发生率明显降低,机体情况恢复较佳,因而围术期生活质量得到明显提升<sup>[15]</sup>。且患者的血糖情况改善,生活质量提高,也使其及家属对临床干预和内镜检查术的满意度得到明显提升。综上所述,糖尿病患者内镜检查术围术期采用以生命帮助计划为基础多学科协作的综合干预能够有效改善血糖、血红蛋白水平,降低围术期低血糖发生率,改善患者生活质量和对内镜检查术满意度。

## LncRNA XR\_001746082 与 miR-135a-5p 互作调控影响胃粘膜癌变的分子机制研究

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目的:检测慢性浅表性胃炎(CSG)、慢性萎缩性胃炎(CAG)、肠上皮化生(IM)、异型增生(Dys)及胃癌(GC)组织中非编码 RNA(ncRNA)的表达谱,研究 LncRNA XR\_001746082 和 miR-135a-5p 对胃癌恶性生物学行为的影响,探讨两者互作影响胃粘膜癌变的机制,为胃癌早期干预提供理论依据及靶点分子。

材料:CSG、CAG、IM、Dys、GC 组织标本;胃癌细胞株 AGS、MKN45。

方法:取病理诊断为 CSG、CAG、IM、Dys 及 GC 的组织标本行 ncRNA 通量测序,筛选癌变过程中差异表达的 ncRNA,用 qRT-PCR 验证;用过表达质粒、miRNA 模拟物或慢病毒分别转染胃癌细胞构建 LncRNA XR\_001746082 和 miR-135a-5p 过表达胃癌细胞株,EdU、CCK-8 和集落形成检测细胞的增殖能力,Transwell 检测细胞的迁移和侵袭能力;RNA Pull Down 及 Western Blot 检测 miR-135a-5p 的靶基因 KHDRBS1;构建过表达 LncRNA XR\_001746082 的裸鼠皮下瘤模型并研究其对瘤体大小的影响;荧光原位杂交及生物信息学方法分析 LncRNA XR\_001746082 在细胞内的分布情况以及与 miR-135a-5p 可能的互作关系并在体外证明。

结果与结论:与 CSG 相比,CAG、IM、Dys、GC 组 LncRNA XR\_001746082 明显高表达,而 miR-135a-5p 明显低表达。体内外研究表明,过表达 LncRNA XR\_001746082 可促进胃癌的增殖,而 miR-135a-5p 则可抑制胃癌的增殖、侵袭及转移。生物信息学预测得到两者可能存在互作关系,qRT-PCR 检测发现 LncRNA XR\_001746082 可发挥分子海绵吸附作用抑制 miR-135a-5p 的表达,并可逆转 miR-135a-5p 抑制胃癌细胞增殖的作用。相反,高表达 miR-135a-5p 也可抑制 LncRNA XR\_001746082 对胃癌细胞的促增殖作用。RNA Pull Down 及 Western Blot 得到 miR-135a-5p 可靶向于 KHDRBS1。荧光原位杂交实验得到 LncRNA XR\_001746082 位于细胞核中。在胃粘膜癌变过程中,ncRNA 的表达谱发生了显著变化,高表达的 LncRNA XR\_001746082 和低表达的 miR-135a-5p 可通过互作调控影响胃癌细胞的增殖能力。

## Fecal Microbiota Transplantation Controls Progression of Experimental Autoimmune Hepatitis in Mice by Modulating the TFR/TFH Immune Imbalance and Intestinal Microbiota Composition

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### Introduction

Autoimmune hepatitis (AIH) is a chronic, progressive, and immunologically mediated inflam-

matory liver disease. Our previous study confirmed that dysregulated between TFR and TFH cells might led to the immunopathological process in AIH. However, recent research found that the defensive mechanism maintaining the hepatic immune homeostasis mainly depended on the intestinal microbiota (IM). This intimate relationship exists between the gut and liver was called “gut—liver axis”. Therefore, remodeling the homeostasis between the host and intestinal microorganisms and reversing the disorder between TFR and TFH cell will provide new perspectives for the treatment of AIH. Fecal microbiota transplantation (FMT) is a treatment method that the functional bacteria from a healthy donor feces is transferred into another patient’s gastrointestinal tract through different routes of administration, so as to reconstitute of a healthy microbial ecosystem in the gut. Taken together, these studies indicate that FMT may be a promising method for managing AIH.

#### Methods

Changes in the enteric microbiome were determined by 16S rRNA quantitative PCR in AIH patients. Moreover, we established experimental model of secondary EAH mice harboring dysbiosis (ABx) to analyse the effects of therapeutic FMT administration on follicular regulatory T (TFR) and helper T (TFH) cell imbalances and IM composition in vivo.

#### Results

##### Intestinal Microbiota Dysbiosis in AIH Patients

The quantity of Bifidobacteria, Lactobacillus, Bacteroides and Clostridium leptum in AIH patients were significantly lower than those in the NAFLD patients and HCs, while quantity of Escherichia coli in the AIH patients were significantly higher than those in the NAFLD patients and HCs. We further assessed the presence of bacterial translocation, and found that the levels of serum LPS in AIH patients were significantly higher than those in the NAFLD patients and HCs.

##### Impaired Liver Function and Imbalance of TFR/TFH Cell Were More Serious in EAH Mice Harboring IM Dysbiosis

We employed S100/FCA—induced EAH model treated with broad—spectrum antibiotics (ABx) to investigate the effects of IM dysbiosis on liver functions and TFR/TFH balance. Successful alterations of the IM composition was confirmed as described previously. Compared with the control group and the EAH group, ABx EAH mice had obvious liver injury evidenced by liver edema with a rising liver index and elevated serum levels of ALT, AST and TBIL as well as a decreased serum levels of albumin. Splenocytes were collected from mice at each time point, and flow cytometry was performed to analyze the percentages of TFR and TFH cells. We observed that TFR cells in the ABx EAH group significantly decreased on the days of post—EAH induction. On the other hand, TFH cells in the ABx EAH gradually increased from 7th to 14th days of post—EAH induction compared to the control group and the EAH group.

##### Therapeutic FMT Attenuated Liver Injury, Hypergammaglobulinaemia and Bacterial Translocation in EAH Mice Harboring IM Dysbiosis

To evaluate if FMT might exert beneficial effects in a chronic autoimmune—related liver inflammation similar to that observed in human AIH patients, ABx EAH were subjected to murine fecal microbiota transplantation (mFMT) on 28 consecutive days starting at day 10 antibiotic treatment. Three days before mFMT transplantation, the antibiotic cocktail was replaced by autoclaved tap water. During the course of the treatment, the elevated serum liver enzymes of FMT—treated ABx EAH and EAH group significantly decreased on the 7th, 14th, and 28th days compared with

those in the control group. The histological score was also similar among FMT-treated and untreated group. In addition, the elevated serum IgG of FMT-treated ABx EAH and EAH group significantly decreased on the 28th days compared with those in the control group. Next, we further evaluated the effect of FMT on bacterial translocation, and found that the serum ET and DAO of FMT-treated ABx EAH and EAH group significantly decreased on the 28th days compared with those in the control group.

#### Therapeutic FMT Regulated TFR/TFH Cell Imbalances in EAH Mice Harboring IMDysbiosis

To evaluate the effect of FMT on the expression of TFR/TFH cell, we further examined the impact of therapeutic FMT administration on the frequency of TFR and TFH cells in the spleen tissue of ABx EAH and EAH group. We observed that TFR cells and TFR/TFH ratio in the FMT-treated ABx EAH and EAH group significantly increased, while TFH cells were significantly decreased on the 28th days compared with those in the control group. Furthermore, our data also showed that the liver levels of IL-10, TGF- $\beta$  and FoxP3-mRNA on the 28th days of FMT administration were statistically higher in the ABx EAH and EAH group than in the control group. Conversely, the liver levels of IL-21 and IL-21-mRNA obviously decreased on the 28th days of FMT administration compared with those in the control group.

#### Therapeutic FMT Attenuated Liver Injury in CXCR5-/-EAH Mice

To explore whether the role of FMT in controlling hepatitis progression was achieved by regulating TFR/TFH cell balance, we employed CXCR5-deficient mice, which fail to develop discrete primary follicles. We observed that the levels of serum liver enzymes were significantly higher in PBS-treated CXCR5-/-EAH group than those in PBS-treated control group on the 28th days. Furthermore, our data also showed that the levels of serum liver enzymes did not significantly decrease until the 28th days in FMT-treated CXCR5-/-EAH group, but decreased significantly on the 7th days in FMT-treated EAH group.

#### Therapeutic FMT Restored Antibiotic-Induced IMDysbiosis in EAH Mice

To assess whether the reduction of liver damage in FMT-treated mice was associated with changes in the IM composition, fecal samples of untreated and FMT-treated mice were analyzed. Compared with the control group, the quantitative amounts of Bifidobacterium and Lactobacillus were significantly increased, and Escherichia coli was significantly reduced on the 28th days in FMT-treated group. Furthermore, the quantitative amounts of Clostridium leptum of FMT-treated group did not differ from that of EAH group.

#### Conclusion

Our findings demonstrated that FMT was capable of controlling hepatitis progression in EAH mice, and the associated mechanism might be involved in the regulation of the TFR/TFH immune imbalance and the restoration of IM composition.

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# Exploration the significance of Tfh and related molecules on C57BL/6 mice model of experimental autoimmune hepatitis

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## Introduction

Autoimmune hepatitis (AIH) is a group of chronic liver diseases characterized by immune-mediated liver pathological damage and liver dysfunction. Over the years, with the advancement of medical treatment technology and the deepening of clinical research, research on AIH has made certain progress. Unfortunately, its pathogenesis is still not fully understood, which may involve complex interactions between genetic susceptibility, environmental predisposing factors, autoantigens, immune disorders, etc, ultimately causing impaired immune tolerance mechanisms. T follicular helper (Tfh) cells are a new class of effector CD4+ T cell subsets, mainly distributed in lymphoid follicles, and is crucial to the differentiation of B lymphocytes and the secretion of immunoglobulins. Besides, IL-21, the major functional molecules of Tfh cells, is involved in regulating B cell differentiation, maturation, and antibody transformation. Therefore, it is of great significance to further study the mechanism of Tfh and its related molecules on AIH. In this study, we used susceptible animal C57BL/6 mice as experimental models to explore the expression and significance of T follicular regulatory (Tfr) cells, Tfh and effector B cells in experimental autoimmune hepatitis (EAH) model.

## Methods

C57BL/6 mice in experimental group were administered by intraperitoneal injection after fully emulsified on 1st day and 7th day with 0.5 mL of 0.5–2.0 g/L S-100 and an equal volume of Buddha Complete Adjuvant (CFA). The levels of serum alanine transaminase (ALT), aspartate aminotransferase (AST), and interleukin-21 (IL-21) were tested by the corresponding kit. Tfr, Tfh and B cell subsets were quantified by flow cytometry. Histological pathology was completed by pathological section experiments.

## Results

### The levels of serum ALT and AST

Serological test revealed that during 1–6 weeks of administration, ALT and AST expressions in EAH model mice (in the 4th week, ALT:  $211.87 \pm 29.57$ ; AST:  $748.23 \pm 26.21$ ) were significantly higher than those in normal saline control group (ALT:  $90.58 \pm 8.98$ ; AST:  $269.40 \pm 13.91$ ), which reached a peak at the 4th week.

### Histological pathology

Histopathological section results showed that the normal control group exhibited complete hepatic lobule structure, neat arrangement of hepatic cords, clear and complete morphology of hepatic cells in the portal area and around the central vein, and no necrotic cells. While in the EAH model

group, the hepatic lobules and hepatocyte cords were severely disorganized, the hepatic cell structures were severely damaged in the portal area and near the central vein, and dispersed inflammatory cell infiltration which was most obvious in 4th week.

#### Detection of TFR, TFH and B cell subsets in liver tissue

To further determine the potential role of different subsets of B and T cells in the pathogenesis of EAH, flow cytometry analysis was proceed, which revealed that the numbers of CD27+CD19+ activated B cells in EAH models were significantly greater than that in the control group, especially in 4th week. Additionally, the chemokine receptor CXCR5 is expressed by both Tfh and Tfr cells and is the defining marker for follicular T cells. And peripheral blood CD4+CXCR5+ T cells were considered as peripheral memory Tfh cells, while FoxP3+ICOS+ T cells were considered as peripheral memory Tfr cells. In EAH model, Tfh cells were lower than healthy control group and Tfr cells were much higher. There was a statistically significant difference between the groups ( $P < 0.01$ ).

#### Elevation of IL-21 expressing level in EAH model

The level of IL-21 in peripheral blood of healthy control group was  $213.18 \pm 148.62$  ng/L, while that in the healthy control group was  $472.96 \pm 205.93$  ng/L. There was a statistically significant difference between the groups ( $P < 0.01$ ).

#### Expression of FoxP3+ and IL-21+ mRNA

Consistent with the previous results, the ratio of Foxp3 and IL-21 in peripheral blood of EAH model mice was significantly higher than that of the healthy control group, and presented a time-dependent pattern.

#### Conclusion

The results of liver pathological changes and serum index changes were similar to the chronic and progressive pathogenesis and pathology of AIH patients, providing a detailed pathological basis for the basic research and clinical experiments of AIH.

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## 内镜下全层切除术在直径 $\leq 10$ mm 直肠神经内分泌瘤治疗效果的研究

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目的:比较分析内镜下全层切除术(EFTR)与内镜下粘膜剥离术(ESD)在治疗直径 $\leq 10$ mm 直肠神经内分泌瘤的治疗效果。方法 选取 2017 年 1 月至 2021 年 10 月于南京医科大学附属淮安第一医院行直肠神经内分泌瘤(NETs)切除术中直径 $\leq 10$ mm 的直肠 NETs 的 49 例患者为研究对象,其中 EFTR 组 21 例,ESD 组 28 例,比较两组病灶大小、操作时间、组织学完全切除率、住院费用、住院时间等。

结果:EFTR 组和 ESD 组患者的年龄、性别以及病灶小在组间均衡。两组术中、术后均无出血、继发感染。EFTR 组及 ESD 组手术操作时间相近,差异无统计学意义。EFTR 组的组织学完全切除率 100%(21/21),ESD 组的组织学完全切除率 82.1%(23/28),差异具有统计学意义。EFTR 组的住

院费用及住院时间均与 ESD 组相似,差异无统计意义。

结论:EFTR 在切除 $\leq 10\text{mm}$  直肠 NETs 的治疗中术中、术后出血及继发感染风险低,组织学完整切除率较 ESD 组高,是一种安全、有效的手术方式。