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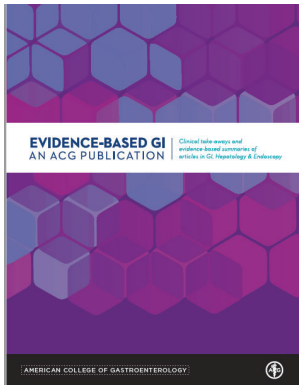

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HEPATOLOGY

Fueling the Failing Liver—ACG Clinical Guideline: Malnutrition and Nutritional Recommendations in Liver Disease

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This summary reviews Singal AK, Wong RJ, Dasarathy S, Abdelmalek MF, Neuschwander-Tetri BA, Limketkai BN, Petrey J, McClain CJ. ACG Clinical Guideline: Malnutrition and Nutritional Recommendations in Liver Disease. Am J Gastroenterol 2025;120:950–972.

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Keywords: guideline, liver disease, nutrition

STRUCTURED ABSTRACT

Question: What are the appropriate methods for assessing malnutrition in patients with chronic liver disease, and what nutritional therapies are recommended across different stages of chronic liver disease?

Design: The guideline was developed by hepatology experts under the ACG Practice Parameters Committee using PICO questions and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to assess evidence strength and develop recommendations.[1] Both recommendation statements and expert key concepts are included.

Patients: Adults with chronic liver disease, including those with cirrhosis, alcohol-associated liver disease, and metabolic dysfunction-associated steatohepatitis (MASH).

Exposure or Interventions: The guideline recommends adequate caloric and protein intake, late-evening carbohydrate snacks, plant-based or branched chain amino acids (BCAA)-enriched protein sources, and avoidance of unnecessary protein restriction. Micronutrient repletion (zinc, vitamin D), vitamin E for MASH, and regular coffee intake are also suggested. Enteral nutrition is preferred over parenteral when oral intake is insufficient.

Outcomes: Through individualized nutritional interventions and disease-specific dietary strategies, patients with chronic liver disease can improve their nutritional status, reduce their risk of complications (e.g., hepatic encephalopathy, infections, and ascites), enhance their muscle mass, improve their quality of life, and reduce their short—and long-term mortality.

Data Analysis: Recommendations were developed through a structured literature review of studies assessing nutritional interventions in liver disease. The GRADE framework was used to assess the quality of evidence and strength of recommendations. Where evidence was insufficient for formal grading, expert consensus informed clinical guidance. Recommendations are categorized as strong or conditional based on benefit-risk assessment, certainty of evidence, feasibility, and patient-centered values.

Funding: This guideline was funded by the ACG. No external commercial support was provided, and all guideline panel members completed conflict of interest disclosures in accordance with ACG policy. The development process was overseen by the ACG Practice Parameters Committee to ensure methodological rigor and independence.

Results: The 2025 ACG Clinical Guideline on Malnutrition and Nutritional Recommendations in Liver Disease provides evidence-based guidance for optimizing nutritional assessment and therapy across a spectrum of chronic liver diseases. Recommendations and selected key supporting evidence are summarized in **Table 1**. The guideline emphasizes the importance of early and routine nutritional screening in patients with chronic liver disease, including cirrhosis, highlighting that malnutrition and sarcopenia are prevalent and worsen with increasing liver disease severity. In hospitalized patients with cirrhosis, early oral or enteral nutrition (EN)

Statement	Quality of Evidence/Strength of recommendation	Key Supporting Evidence
1. Suggest initiating early oral or enteral nutrition in hospitalized patients with cirrhosis	Low/Conditional	Three RCTs and 2 cohort studies[2-6] showed that starting oral/enteral feeds within 48 h increased calorie/protein delivery, shortened hospital/ICU stay, and reduced in-hospital mortality by ≈30%
2. Suggest implementation of nutritional supplementation therapy in patients with cirrhosis or alcohol-associated hepatitis	Very Low/ Conditional	In AH, daily 1-month adequate caloric intake in VA trials correlated with 6-month survival; EN improved bilirubin, antipyrine clearance, and reduced 1-year mortality vs prednisone; intake <21.5 kcal/kg/day or <77.6 g protein/day predicted worse outcomes[7-9]
3. Suggest use of natural vitamin E (800 IU/day) in patients with MASH without cirrhosis	Low/Conditional	PIVENS (adults) and TONIC (children) RCTs showed 800 IU/day d-α-tocopherol for 96 wk improved steatosis, ballooning, and inflammation in 43%-58 % vs 19%-28% on placebo, with ALT normalization in >50%[10-12]
4. Suggest intake of ≥2 cups of coffee/day in chronic liver disease to reduce fibrosis risk progression and HCC development	Low/Conditional	Large prospective cohorts (>200,000 subjects) demonstrated dose-responsive 25%-40% reductions in advanced fibrosis and 50% lower HCC incidence among drinkers of ≥2 cups/day, independent of alcohol and obesity[13-15]
5. No recommendation for or against strict sodium restriction in patients with cirrhosis and ascites managed with diuretic therapies	Insufficient	Two small RCTs (≤60 patients) comparing 2g vs unrestricted sodium showed inconsistent effects on ascites control, hyponatremia, and QoL; both with high bias risk[16, 17]
6. Recommend against protein restriction in decompensated cirrhosis with HE	Very Low/ Conditional	Four crossover studies showed ≤0.6 g/kg protein worsened nitrogen balance and muscle loss without HE improvement; reintroduction of 1.2 g/kg improved cognition[18,19]
7. Suggest vegetarian protein sources in cirrhosis with HE when supplementation is needed	Low/Conditional	Plant-based protein lowers ammonia via higher arginine/fiber content. Four studies have shown clinical improvement with vegetarian protein. A RCT (120 patients) found vegetable protein improved minimal HE (71% vs 23%) and reduced HE risk (10% vs 22%)[20,21]
8. Recommend adding branched-chain amino acids to standard therapy in patients with cirrhosis and HE	Moderate/Strong	BCAA deficiency impairs ammonia detoxification via muscle. BCAA supplementation improves muscle mass, reduces ammonia, and enhances glutamine synthesis. A Cochrane meta-analysis of 16 RCTs (n=827) found oral BCAAs improved HE (RR 0.67); after excluding lactulose/neomycin controls, reduced mortality (RR 0.76); IV BCAAs showed no benefit[22,23]
9. Recommend incorporating a late-evening snack in cirrhosis to improve BMI, lean mass, and reduce ascites/HE	Moderate/Strong	Outpatient nutrition therapy improves survival and reduces hospitalizations in cirrhosis. Late evening snacks (≈710 kcal) reduce protein catabolism and improve nitrogen balance, with meta-analyses showing improved liver function and fewer complications (ascites, HE); effects on muscle mass and survival remain inconsistent[24, 25]

Table 1. Summary of recommendations with supporting evidence.

AH, alcohol associated hepatitis; BCAA, branched chain amino acids; BMI, body mass index; EN, enteral nutrition; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; ICU, intensive care unit; IV, intravenous; MASH, metabolic dysfunction-associated steatohepatitis; RCT, randomized controlled trial; RR, relative risk; VA, Veterans Administration.

within 48 hours is associated with improved protein-calorie delivery, reduced hospital length of stay, and lower in-hospital mortality (approximately 30% reduction). In patients with alcohol associated hepatitis (AH), nutritional support, particularly through enteral supplementation, has been shown to improve liver function markers and reduce 1-year mortality compared to corticosteroid therapy, mainly by lowering infection rates. Furthermore, lower caloric and protein intake thresholds (less than 21.5 kcal/kg/day and less than 77.6 g/day) independently predict worse outcomes in this population.

In the outpatient setting, structured nutrition counseling and frequent small meals or late evening snacks (high-complex carbohydrate ~200 kcal) are associated with improved nitrogen balance, reduced sarcopenia, and a decreased incidence of hepatic encephalopathy (HE) and ascites. These benefits are demonstrated in multiple studies and meta-analyses, although evidence on survival impact remains limited.

The guideline advises against protein restriction in patients with HE. Instead, diets enriched in vegetarian protein sources may be beneficial due to their favorable effects on ammonia metabolism and neurotoxins. Supporting evidence from older but consistent RCTs indicates reduced ammonia levels and improved psychometric scores. Similarly, supplementation with BCAAs in HE improves the resolution of symptoms (relative risk [RR] 0.67 with oral BCAA) and reduces mortality when compared to standard therapy alone (RR 0.76 after exclusion of lactulose/neomycin controls). BCAAs also enhance muscle mass and ammonia detoxification.

Vitamin and mineral supplementation is addressed with conditional recommendations. Vitamin D deficiency is common in cirrhosis and is associated with infections, spontaneous bacterial peritonitis, and mortality. While evidence is limited, supplementation improves biochemical profiles and Child-Pugh class. Zinc replacement is also recommended in individuals with low serum zinc levels or those with symptoms of deficiency. The guideline also supports ≥2 cups/day of coffee to reduce fibrosis progression and hepatocellular carcinoma risk in chronic liver disease.

Lifestyle interventions, including diet and exercise, are endorsed for patients with MASH to reduce disease progression and improve metabolic outcomes, despite limited data on fibrosis reversal. Sodium restriction in cirrhosis with ascites remains inconclusive due to conflicting trial results. These findings support a paradigm shift toward early, individualized, and proactive nutritional management in liver disease to improve patient outcomes across inpatient and outpatient settings.

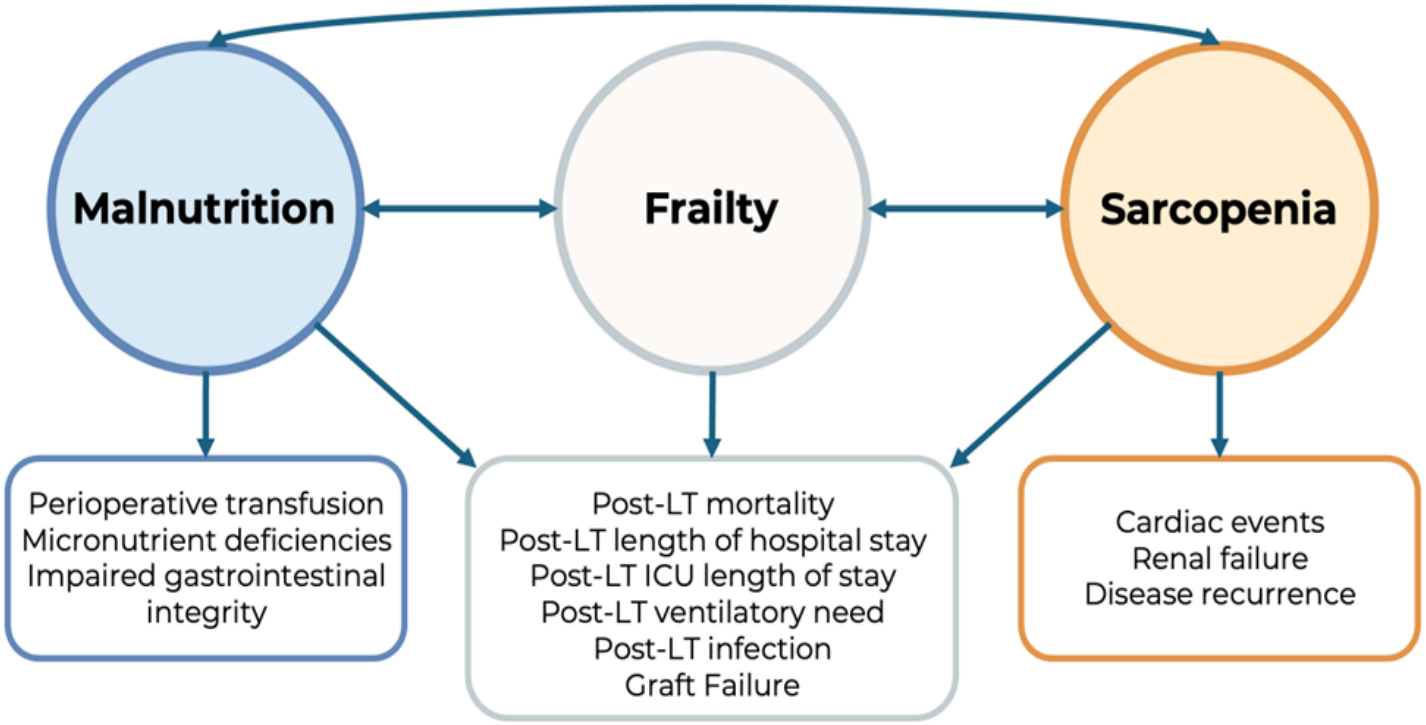

Figure 1. The impact of malnutrition, frailty, and sarcopenia in end-stage liver disease. LT, liver transplantation; ICU, intensive care unit. Adapted from Duong et al.[26]

COMMENTARY

Why Is This Important?

Malnutrition and sarcopenia are highly prevalent and underrecognized, affecting 20% of patients with compensated cirrhosis and up to 60% in those with decompensated cirrhosis and are strongly linked to morbidity, mortality, and poor transplant outcomes (**Figure 1**). Malnutrition, sarcopenia, and frailty are not interchangeable terms, though they are linked. A review written by Duong et al highlights these concepts in detail.[26]

This guideline reflects a growing understanding that structured nutritional assessment and individualized therapy are essential across the spectrum of liver disease. It marks the first ACG guideline dedicated to nutrition in liver disease, addressing gaps in both inpatient and outpatient management.

Key Study Findings

The guideline strongly recommends adding BCAAs to standard therapy in patients with cirrhosis and HE, given evidence supporting improved HE resolution and reduced mortality.

A late-evening snack is also strongly recommended to enhance body mass index, preserve lean muscle mass, and decrease the incidence of ascites and HE. Early oral or EN is advised for hospitalized cirrhosis patients to improve protein-calorie delivery and lower in-hospital mortality. Protein restriction is discouraged in decompensated cirrhosis with HE, and vegetarian protein sources may be preferred when supplementation is necessary due to their favorable effects on ammonia metabolism.

Additional conditional suggestions include nutritional supplementation in alcohol-associated liver disease, vitamin E supplementation in MASH without cirrhosis, and daily coffee intake to reduce fibrosis progression and HCC risk.

Caution

Some recommendations considered low or very low-quality evidence of older studies with small sample sizes. While findings support proactive nutrition management, the evidence base remains limited for some outcomes, particularly long-term survival.

My Practice

Vital signs are just that—vital. It would be unthinkable to see a patient without first reviewing their vital signs, whether in an outpatient or inpatient setting. From my perspective, assessing and understanding a patient's nutritional status should be viewed similarly, especially in those with chronic liver disease.

Evidence clearly shows that the severity of malnutrition correlates with the progression of liver disease. Sarcopenia, likewise, impacts outcomes throughout the transplant continuum. Yet, despite this well-established knowledge, I am often surprised when new patients express that no one has discussed fundamental nutrition goals with them—such as high protein intake, late-night protein snacks, coffee consumption, exercise, and limitations on salt intake.

While counseling patients takes time and deliberate effort, it is both essential and worthwhile, particularly during the initial visit. I approach nutrition counseling as an ongoing conversation rather than in isolation. I focus on small, achievable changes, explaining that progress—not perfection—is the goal. Encouraging even 1-3 changes between visits can lead to significant improvements over time.

Adapting my approach to the patient's understanding is crucial. When a patient struggles to grasp the rationale, I simplify my explanations; when a patient is

well-informed, I elevate the discussion. Cultural competence and flexibility are key to effective communication.

In the ideal situation, access to a strong multidisciplinary team that includes registered dieticians is instrumental to a patient-centered practice. Separate, dedicated teams for the general hepatology and transplant populations are also ideal, given the often varying needs of these unique cohorts.

Understandably, accessing a dietitian can often be cost-prohibitive as it is where I currently practice. Thus, I recently met with our dietitians to create a patient-friendly "Mediterranean diet" handout that is easily accessible in our clinic. I find that patients enjoy having a physical handout, allowing them to start making small dietary changes either before they meet with the dietitian or, if they cannot afford it, to utilize this handout as a starting point in their own journey to achieve their personal weight goals. Ensuring that such patient materials are available in multiple languages is key to providing culturally competent care. As a final point, in the Bay Area, where I live and practice, there is a fair number of patients with lean MASH. These patients are certainly some of the more challenging cases to care for due to the limited therapeutic options. In these instances, I have often recommended Vitamin E. I very seldom recommend BCAAs and acknowledge the variability in this practice among my colleagues.

In summary, we should continue to consider nutrition assessment as the fifth vital sign. To ensure equitable and inexpensive access to nutrition assessment, I suspect the future will leverage AI and serum biomarkers—or at least that is the hope!

For Future Research

According to the guideline, future research should focus on validating accessible biomarkers for sarcopenia using proteomic and metabolomic approaches and clarifying the therapeutic role of dysbiosis-targeted strategies beyond HCC.

Intervention trials are needed to assess whether reducing simple sugars benefits patients with cirrhosis and visceral adiposity. The optimal type, intensity, and impact of exercise before and after liver transplantation remains under investigation.

Additionally, the long-term effects of vitamin D supplementation on cirrhosis progression and HCC are still unknown. More evidence is also needed to confirm whether lifestyle modification can truly reverse hepatic fibrosis.

Conflict of Interest

The authors have no conflicts of interest to disclose.

Abbreviations

AH, alcohol associated hepatitis; AI, artificial intelligence; BCAA, branched chain amino acids; EN, enteral nutrition; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; ICU, intensive care unit; LT, liver transplantation; MASH, metabolic dysfunction-associated steatohepatitis; RCT, randomized controlled trial; RR, relative risk.

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EVIDENCE-BASED GI
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Can We Avoid Colonoscopies in Lynch Syndrome?

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Associate Editor

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COLON

This summary reviews van Liere D, de Boer N, van Leerdam M et al. Fecal Immunochemical Test to Detect Colorectal Neoplasia in Lynch Syndrome: A Prospective Multicenter Study. Am J Gastroenterol 2025;120(3): 632-641.

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Keywords: fecal immunochemical tests; colonoscopy; Lynch syndrome

STRUCTURED ABSTRACT

Question: Can the fecal immunochemical test (FIT) extend colonoscopy surveillance intervals?

Design: Prospective multicenter observational study.

Setting: Five hospitals in the Netherlands.

Patients: Lynch syndrome patients with a pathogenic germline variant in *MLH1, MSH2/EPCAM, MSH6,* or *PMS2* due for surveillance colonoscopy (typically every 2 years starting at age 25 per Dutch guidelines). They excluded those with extended/total colectomy, incomplete colonoscopies, colonoscopies with inadequate bowel preparation quality or withdrawal <6 minutes, and colonoscopies with any mucosal inflammation/infection or polypectomy without

pathology report. They also excluded those who used bowel preparation within 7 days before FIT.

Exposure or Interventions: FIT (SENTiFIT—fecal occult blood [FOB] gold test (Sentinel Diagnostics, Milan, Italy) administered 3 months before surveillance colonoscopy

Outcomes: Colonoscopic findings of various types of any relevant neoplasia (colorectal cancer [CRC], advanced polyps, non-advanced polyps), advanced neoplasia (CRC, advanced polyps), or CRC + advanced adenoma compared to a control of no neoplasia or non-advanced serrated lesions.

Data Analysis: Descriptive analysis of baseline characteristics. Diagnostic performance of FIT measured by sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and area under the curve. Number needed to diagnose any neoplasia.

Funding: Dutch Digestive Foundation.

Results: Of 217 Lynch syndrome (LS) patients, 35 (16%) had *MLH1*, 56 *MSH2/EPCAM*, 70 *MSH6*, and 56 *PMS2* variants. Median age was 51, 15% had personal history of CRC, and 185 (85%) did not have any prior colon resection. Thirty-two percent had any neoplasia, 5 (2.3%) had advanced adenoma(s) all by size ≥10 mm, 4 had advanced serrated lesions (three-quarters by size ≥10 mm), and 4 (1.8%) had CRC, all of which were stage I or II. Two of the CRCs were found on index colonoscopy, and 2 after a delayed colonoscopy surveillance interval of 5-6 years. The advanced polyps were distributed throughout the colon.

At a FIT threshold of 2.5 ug Hgb/g feces, FIT had 26% sensitivity, 91% specificity, and 72% NPV for any relevant neoplasia, and 69% sensitivity, 91% specificity, and 97.1% for advanced neoplasia. At a threshold of 4.1 ug Hgb/g feces, FIT had 21% sensitivity, 94% specificity, and 71% NPV for any relevant neoplasia, 69% sensitivity, 94% specificity, and 97% NPV for advanced neoplasia, and 89% sensitivity , 94% specificity, and 99% NPV for CRC + advanced adenoma. For every 100 FIT tests at the 4.1 threshold, 11 patients would test positive but 2 with advanced neoplasia would be missed.

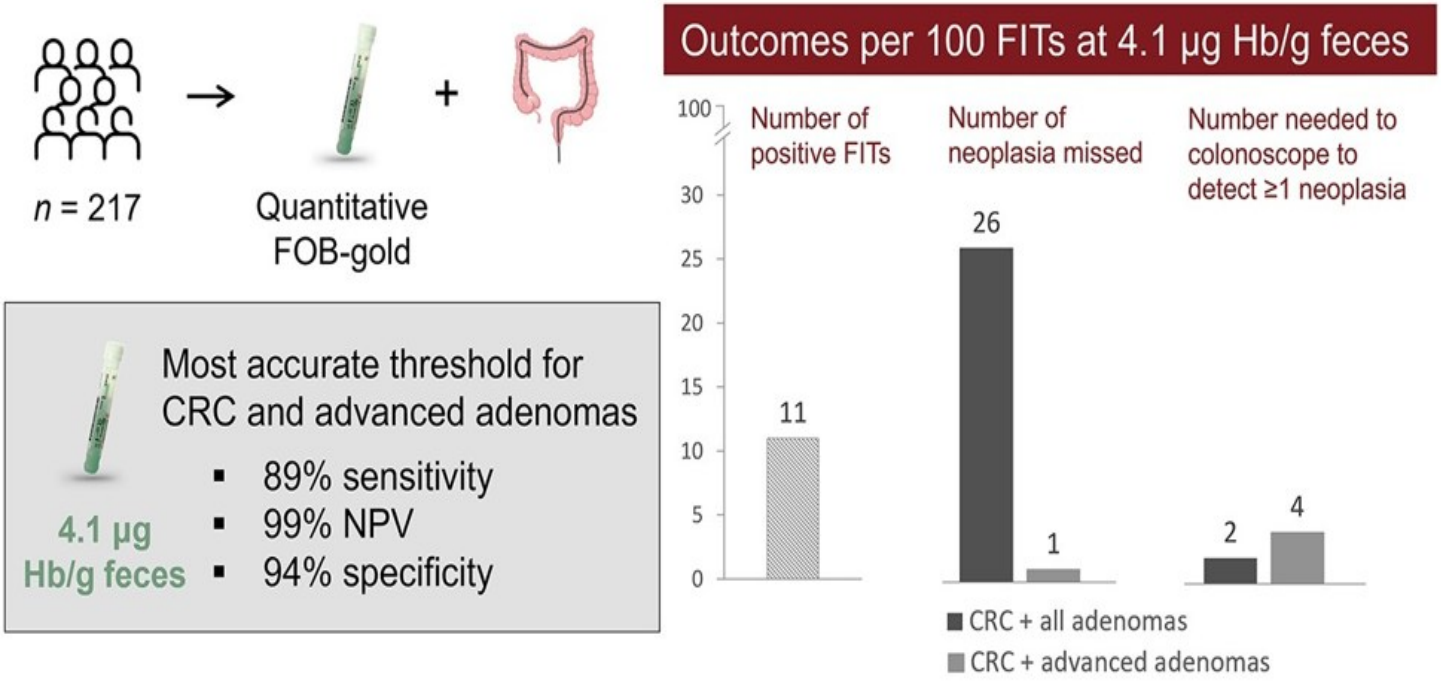

Figure 1. Visual abstract for FIT for surveillance in Lynch syndrome.

CRC, colorectal cancer; FIT, fecal immunochemical test; FOB, fecal occult blood; NPV, negative predictive value.

COMMENTARY

Why Is This Important?

Similar to other chronic diseases/diagnoses (polyposis syndromes, inflammatory bowel disease) that warrant frequent colonoscopy, the cumulative colonoscopic burden on both the affected individual patient and the healthcare system is significant, particularly in resource-limited settings. FIT continues to be explored as an inexpensive, non-invasive method to decrease colonoscopic burden and/or prioritize colonoscopy for those who benefit most in both average-risk and elevated-risk populations.[1,2] LS patients have one of the heaviest colonoscopic burdens, often requiring them annually.[3]

Key Study Findings

At the 4.1 ug Hgb/g feces threshold, FIT had a reasonable diagnostic accuracy for detection of colorectal cancer or advanced adenoma, although sensitivity was worse when the addition of sessile

For every 100 FIT tests, we would miss 2 LS patients with advanced neoplasia (cancer or advanced polyp). This is an intriguing study that raises the possibility that FIT, or alternative non-invasive tests, could be used as an adjunct to screening/surveillance colonoscopy in some respect for LS patients in the future.

Caution

In the United States, FIT is not commonly standardized or calibrated to specific fecal hemoglobin concentrations, thus cannot be readily used in daily practice at this current time. Even with proper calibration there are medicolegal implications of delaying gold-standard colonoscopy in the absence of more definitive evidence to change our national guidelines.[3]

My Practice

I personally am not yet comfortable extending surveillance intervals longer than recommended by National Comprehensive Cancer Network guidelines.[3] In terms of how we can make an impact on the burden of colonoscopy as providers, the bowel preparation process is often the most cumbersome step in the process. In addition to split bowel preparation, I favor prescribing low-volume or tablet bowel preparation products which is commonly covered by most insurances. Gummy bears (other than red/purple colors) are also considered a clear liquid and can help with the hunger during fasting.

In addition, we should not lose sight of the ultimate goal- prevention and risk reduction of colorectal cancer. I typically prescribe/recommend aspirin prophylaxis in LS of all genotypes. This is recommended by National Comprehensive Cancer Network guidelines (notably was not standard in Dutch guidelines for this study),[3] because it has been shown to substantially decrease colorectal cancer incidence over the course of decades.[4] Whether this itself is enough to extend surveillance intervals in select LS patients remains to be seen.

For Future Research

There are many future avenues with potential to decrease colonoscopic burden among LS patients. Given the high incidence of colorectal cancers, which does vary by affected gene, we will need to study a larger number of patients for each LS genotype powered for a wide range of risk profiles such as aspirin usage, personal history of CRC (most did not have prior CRC in this study) which portends higher metachronous CRC risk,[5] and family history of CRC. In addition, multitarget stool DNA tests have higher diagnostic accuracy than traditional FIT with broad payer coverage, and may have a larger impact in this high-risk population.

Conflict of Interest

The author has no conflicts of interest.

Abbreviations

CRC, colorectal cancer; FIT, fecal immunochemical test; FOB, fecal occult blood; LS, Lynch syndrome; NPV, negative predictive value; PPV, positive predictive value.

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EVIDENCE-BASED GI
AN ACG PUBLICATION

Sphincterotomy to Prevent PEP After FCSEMS placement

ENDOSCOPY

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This summary reviews Onnekink AM, Gorris M, Bekkali NL on behalf of the Dutch Pancreatic Cancer Group, *et al.* Endoscopic sphincterotomy to prevent post-ERCP pancreatitis after self-expandable metal stent placement for distal malignant biliary obstruction (SPHINX): A multicentre, randomised controlled trial. *Gut* 2025;74:246-254.

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Keywords: ERCP pancreatitis, malignant biliary obstruction, RCT

STRUCTURED ABSTRACT

Question: Does endoscopic sphincterotomy prior to fully covered self-expanding metal stent placement (FCSEMS) reduce the risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) in patients with suspected distal malignant biliary obstruction (MBO)?

Design: Multicenter, randomized, open-label, controlled superiority trial.

Setting: Seventeen hospitals (16 Dutch and 1 Spanish hospital including academic and teaching centers).

Patients: Adults aged 18 years or older with suspected distal MBO undergoing

ERCP with FCSEMS placement. Two hundred and ninety-seven patients were randomized (156 to sphincterotomy and 141 to control). Exclusion criteria included benign biliary stenosis, prior sphincterotomy, hilar obstruction, prior pancreatic duct (PD) stenting, coagulopathy, or inability to stop anticoagulants.

Exposure or Interventions: Patients were randomized to either undergo endoscopic sphincterotomy or no sphincterotomy prior to FCSEMS placement. All patients received standard FCSEMS 10 mm in diameter and the majority of patients received stents 6 cm in length. However, 4 cm and 8 cm in length stents were also placed depending on anatomical considerations. Patients also received rectal nonsteroidal anti-inflammatory drugs for PEP prophylaxis. Procedures were performed under direct supervision of expert endoscopists.

Outcomes: The primary outcome was PEP within 30 days, as defined per modified Cotton criteria: (1) onset of new or worsened abdominal pain requiring new or prolonged hospital admission and (2) an elevation of pancreatic enzymes (amylase and/or lipase) of ≥3 times upper limit of normal at more than 24 hours after the procedure.[1] Secondary outcomes included severity of PEP, technical success, bleeding, perforation, cholangitis, cholecystitis, stent-related morbidity, and 30-day mortality.

Data Analysis: Intention-to-treat and per-protocol analyses were conducted. Categorical variables were compared using Fisher's exact test, and continuous variables compared with Student's *t*-test or Mann-Whitney U test. Relative risk (RR) with 95% confidence intervals (CIs) were reported. Interim analysis was performed and the study was terminated early due to futility.

Funding: Cook Medical Europe partially reimbursed stents but had no role in the study design, data collection, analysis, or manuscript preparation.

Results: Overall, 297 patients were included in the intention-to-treat analysis, with 156 in the sphincterotomy group and 141 in the control group. PEP occurred in

17% of sphincterotomy vs 21% of control patients (RR 0.78, 95% CI 0.49–1.26; *P*=0.37). There were no significant differences in bleeding, perforation, cholangitis, or cholecystitis. 30-day mortality was 6% vs 4%. The study was terminated early after interim analysis showed futility.

COMMENTARY

Why Is This Important?

PEP is the most common adverse event of ERCP, and rates are high—especially due to FCSEMS placement. This is hypothesized to be the result of pancreatic outflow obstruction caused by the radial forces of the FCSEMS on the orifice of the PD.[2] While endoscopic sphincterotomy is frequently performed to reduce this risk, high-quality prospective evidence validating its benefit in the context of FCSEMS placement is lacking. The SPHINX trial attempts to address this gap through a randomized controlled design and provides important data to inform best practices in managing patients with distal MBO undergoing ERCP.

Key Study Findings

The trial demonstrated that endoscopic sphincterotomy before FCSEMS placement did not significantly reduce the risk of PEP compared to no sphincterotomy. The rates of PEP were 17% vs. 21% (RR 0.78, *P*=0.37), and no significant differences were found in adverse events such as bleeding, perforation, cholangitis, or cholecystitis.

Caution

The results of the study need to be interpreted with the following caveats. This study was terminated early due to futility and slower-than-expected enrollment, which reduced statistical power to detect more modest differences. Additionally, patients who could not undergo randomization due to technical difficulties during ERCP (e.g., pre-cut sphincterotomy or prophylactic PD stenting) were excluded, potentially limiting generalizability. In addition to these factors, the rate of PEP in this study are extremely high (17% and 20% in both groups). These rates are high especially considering the population included in this study, patients with suspected distal MBO, are typically not considered as high-risk patients for PEP. Also, incidental PD cannulation was seen in 33% of patients in the sphincterotomy group compared to 28% of patients in the control group, which is a known risk factors for PEP.[3]

There was no mention of PD stent placement in these patients which is a critical intervention shown to reduce the rates of PEP.[4] It would have been interesting to see if PD stents were placed in patients where deep PD guidewire cannulation was achieved, and if there was any difference in PEP rates. Also, a subgroup analysis excluding patients where PD cannulation was achieved would have also provided valuable insight. Lastly, the risk of biliary sphincterotomy in this cohort of patients is low. The main risks of biliary sphincterotomy are bleeding and perforation and both these adverse events can be treated with FCSEMS placement.[5,6] Therefore, whether the performance of sphincterotomy in the vast majority of these patients with MBO adds additional risks is unclear.

My Practice

My practice for patients with MBO who need a FCSEMS does not change significantly with the results of this trial. The high rates of PEP in this trial are unclear and could be attributed to the fact that only <50% of ERCPs were characterized as easy cannulations. Another factor highlighted by the authors is variable operator experience of endoscopists performing ERCP. My practice in these cases where PD is cannulated is to place a small caliber PD stent with features that would allow spontaneous passage of PD stent to reduce the risk of PEP.

In addition, as this randomized controlled trial shows that there was no difference in rate of other adverse events in both groups, my practice of performing a biliary sphincterotomy in these patients unless sphincterotomy is higher risk (in patients with coagulopathy, bleeding disorders or those in which anticoagulation cannot be stopped) will not change. Lastly, 4% of patients who developed PEP in this study died of severe acute pancreatitis. Therefore, in summary, this study reinforces that placement of FCSEMS in MBO carries a higher risk of PEP and this should be incorporated in consent considerations.

For Future Research

Future research is needed to compare the impact of PD stent placement on reduction of PEP in patients with MBO undergoing FCSEMS placement.

Conflict of Interest

Dr. Bilal is a consultant for Boston Scientific, Steris Endoscopy, Aspero Medical and Cook Medical.

Abbreviations

CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; FCSEMS, covered self-expanding metal stent placement; MBO, malignant biliary obstruction; PD, pancreatic duct; PEP, Post-ERCP pancreatitis; RR, relative risk.

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EVIDENCE-BASED GI
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IBD Surveillance Colonoscopy: To Spray or not to Spray!

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IBD

This summary reviews Te Groen M, Wijnands AM, den Broeder N, et al. Surveillance in inflammatory bowel disease: White light endoscopy with segmental re-inspection versus dye-based chromoendoscopy - a multi-arm randomised controlled trial (HELIOS). Gut. 2025;74(4):547-556.

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Keywords: RCT, IBD, surveillance, chromoendoscopy, neoplasia

STRUCTURED ABSTRACT

Question: Among adult patients with inflammatory bowel disease (IBD) in remission, is high-definition (HD) white-light endoscopy with segmental reinspection non-inferior to HD chromoendoscopy to detect colorectal neoplasia?

Design: Multi-center, open-label randomized controlled trial (RCT) testing non-inferiority.

Setting: Four academic hospitals in The Netherlands.

Patients: Adults aged ≥18 years with colonic IBD (with ≥30% colonic involvement) and ≥8 year disease duration (or any duration if concomitant primary

sclerosing cholangitis). Patients were excluded if there was active inflammation (>20 cm of colonic involvement) or poor bowel preparation (Boston Bowel Preparation Score <6).

Interventions: HD white-light endoscopy on colonoscopy withdrawal, with a second-look segmental re-inspection of each colonic segment. This was compared to single-pass HD white-light endoscopy and HD chromoendoscopy with spraying dye during withdrawal and segmental reintroduction and inspection.

Outcomes: Primary outcome was colorectal neoplasia detection rate (the proportion of patients with macroscopic colorectal neoplasia with pathology finding: indefinite for dysplasia, low-grade dysplasia, high-grade dysplasia, colorectal cancer, sessile serrated adenoma with dysplasia). Secondary outcomes were: total number of resected or biopsied macroscopic lesions per colonoscopy, total number of colorectal neoplasia per colonoscopy, procedure time, withdrawal time, impact of withdrawal time on the colorectal neoplasia detection rate (number of detected neoplasia per 10 minutes of withdrawal time), and number of macroscopic lesions detected during first vs second inspection round for HD white-light endoscopy with reinspection.

Data Analysis: Per-protocol (for the primary analysis) as well as modified intention-to treat analysis. Patients' characteristics and outcomes were summarized using descriptive analysis between the three arms of the study. HD white-light endoscopy with segmental reinspection was compared to HD chromoendoscopy using a non-inferiority analysis, while it was compared to HD white-light single pass endoscopy using a superiority analysis.

Funding: Supported by the Dutch Initiative on Crohn and Colitis, and the "StichtingInnovatie en Kwaliteit Maag, Darm-, Leverziekten" (Tilburg, The Netherlands) (AMW).

Results: Among 666 patients enrolled, 265 were randomized to HD white-light endoscopy with segmental reinspection, 268 to HD chromoendoscopy, and 133 to

single-pass HD white-light endoscopy (median age 48-52 years, 49%-55% male, median disease duration 15-19 years, with 53%-63% with ulcerative colitis, 36%-45% with Crohn's disease).

Colorectal neoplasia was detected in 10.3% with HD white-light endoscopy with segmental reinspection (with 81% of lesions detected during first inspection), 13.1% with HD chromoendoscopy, and 6.1% in single-pass HD white-light endoscopy (**Table 1**). Segmental reinspection was non-inferior to chromoendoscopy (difference -2.8%, with lower boundary of 95% confidence interval (CI) at -7.8% not exceeding the -10% non-inferiority margin, $P<0.01$) but not superior to single-pass endoscopy (difference +4.1%, $P=0.19$). For white-light with reinspection, total number of resected or biopsied lesions per colonoscopy was lower when compared with HD chromoendoscopy (n=123 vs 175, $P<0.01$) and comparable to single-pass endoscopy (n=54, $P=0.32$). For white light with reinspection, withdrawal time was shorter than for chromoendoscopy (-8.0 minutes, $P<0.01$) and longer than for single-pass endoscopy (+4.0 minutes, $P<0.01$). When adjusted for withdrawal time, their detection rates were similar. Results of the modified intention-to-treat analysis (597 patients) were concordant with per-protocol analysis for both primary and secondary outcomes.

	HD White-Light Endoscopy with Segmental Reinspection	HD Chromoendoscopy	Single-Pass HD White-Light Endoscopy
N	**234**	**214**	**115**
Colorectal Neoplasia Detection Rate	10.3%	13.1%	6.1%
Total Lesions Resected/Biopsied	123*	175*	54
Withdrawal Time (mean difference)	Reference (median 19 min)*	+8.0 min*	−4.0 min*
Neoplasia Detection per 10 min (median)	0.062	0.058	0.044
Adjusted Detection Rate (OR)	Reference	OR 0.97 (95% CI 0.92 –1.03, $P=0.34$)	OR 1.03 (95% CI 0.93–1.14, $P=0.56$)

Table 1. Study results.

*statistically significant. CI, confidence interval; HD, high-definition; OR, odds ratio.

COMMENTARY

Why Is This Important?

Patients with IBD are at increased risk of colorectal cancer, which underlines the importance of effective surveillance methods. Dye-based chromoendoscopy has been a key method for improved neoplasia detection, but its use can be limited by procedure time, logistics and expertise of the endoscopists. This trial shows that white-light endoscopy with segmental reinspection may be a practical alternative with comparable results for neoplasia detection. The study suggests that a longer withdrawal time is key rather than the application of a dye for a higher neoplasia detection rate.

Key Study Findings

Among 563 patients, colorectal neoplasia was detected in 10.3% with HD white-light endoscopy with segmental reinspection (with 81% of lesions detected during first inspection), 13.1% with HD chromoendoscopy, and 6.1% in single-pass HD white-light endoscopy.

Segmental reinspection was non-inferior to chromoendoscopy (difference -2.8%, with lower boundary of 95% CI at -7.8% not exceeding the -10% non-inferiority margin, $P<0.01$) but not superior to single-pass endoscopy (difference +4.1%, $P=0.19$).

For white-light with reinspection, total number of resected or biopsied lesions per colonoscopy was lower when compared with HD chromoendoscopy (n=123 vs 175, $P<0.01$) and comparable to single-pass endoscopy (n=54, $P=0.32$). For white light with reinspection, withdrawal time was shorter than for chromoendoscopy (-8.0 minutes, $P<0.01$) and longer than for single-pass endoscopy (+4.0 minutes, $P<0.01$). When adjusted for withdrawal time, their detection rates were similar. Results of the modified intention-to-treat analysis (597 patients) were concordant with per-protocol analysis for both primary and secondary outcomes.

Caution

Limitations include lower than expected neoplasia detection rates with smaller than expected differences between groups which affected the superiority analysis and non-inferiority margin (which could have been set lower). There was also heterogeneity in chromoendoscopy dye (methylene blue or indigo carmine). The drop-out rate was also unexpectedly high at 15% (from initially expected at 5%). Finally, the study did not include HD virtual chromoendoscopy which is becoming a widely used technique (this method was not included in guidelines at the start of this study).

My Practice

Current ACG guidelines recommend using dye-based chromoendoscopy when using standard-definition colonoscopy for IBD surveillance, and recommend either dye-based chromoendoscopy or narrow-band imaging when using HD

colonoscopy, though the body of evidence for these recommendations is rated overall low quality.[1] The American Gastrointestinal Association expert review recommendations state similar recommendations: dye-based chromoendoscopy should be used when using standard-definition colonoscopy or with history of dysplasia, but that virtual chromoendoscopy can be a suitable alternative when using HD colonoscopy.[2]

In our current practice, we use HD virtual chromoendoscopy which was not included in this article but, like HD white-light endoscopy, is also associated with shorter procedure times than dye-based chromoendoscopy (though non-inferiority trials have not been conducted between virtual and dye-based chromoendoscopy). The study supports the use of HD white-light endoscopy with reinspection as a practical alternative given its non-inferiority for neoplasia detection. Importantly, neoplasia detection is still dependent on total withdrawal time, this has been validated across different studies among the general population (non-IBD patients). Therefore, we cannot rely solely on the inspection method alone and should avoid rushed examinations. Adequate withdrawal time remains essential for best lesion detection. White-light endoscopy does however offer the benefit of smoother logistics compared to dye-based endoscopy, which requires comfort with handling dye material and efficient communication between endoscopist and endoscopy staff. This added value will expand access to care for IBD patients to non-IBD experts, thus increasing equity.

For Future Research:

Since the initial planning for the HELIOS trial, HD virtual chromoendoscopy has been included in interval guidelines as summarized above. Future research should focus on comparing HD virtual chromoendoscopy with HD white-light endoscopy with reinspection and HD dye-based chromoendoscopy. There is promising work to be published soon to contribute to the current existing body of evidence on this topic, again suggesting that HD virtual chromoendoscopy can be a strong competing method for surveillance colonoscopy.[3] In addition, cost-effectiveness analysis comparing the different modalities of endoscopy in this patient population is warranted to help formulate stronger recommendations for guidelines on this important topic.

Conflict of Interest

Drs. Chaudhary and Al Kazzi reports no potential conflicts of interest related to this study.

Abbreviations

ACG, American College of Gastroenterology; CI, confidence interval; HD, high-definition; IBD, inflammatory bowel disease; OR, odds ratio; RCT, randomized controlled trial.

Note

The authors of this EBGI summary are active on social media. Tag them to discuss their work.

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