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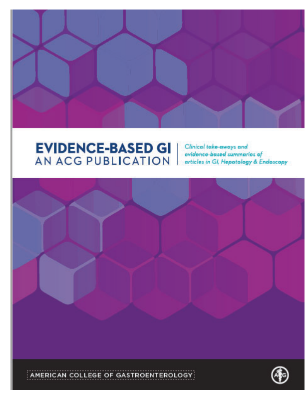

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EBGI Volume 7, Issue 3

June 2026

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A Fully Subcutaneous Guselkumab Regimen is Efficacious and Durable for Moderately to Severely Active Ulcerative Colitis

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This summary reviews Long M, Allegretti JR, Danese S, et al. Efficacy and safety of subcutaneous guselkumab induction therapy in participants with moderately to severely active ulcerative colitis (ASTRO): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Gastroenterol Hepatol. 2026; 11 (4): 284-298.

Correspondence to Elie Al Kazzi, MD, MPH. Associate Editor. Email: EBGI@gi.org

Keywords: ASTRO, double-blind, randomized, placebo-controlled trial

STRUCTURED ABSTRACT

Question: Is subcutaneous (SC) guselkumab induction safe and efficacious for adults with moderately to severely active ulcerative colitis (UC)?

Design: The ASTRO study is a phase 3, double-blind, treat-through, randomized, placebo-controlled trial.

Setting: The study was made in 153 sites, including community centers and hospitals, across 25 countries.

Patients: Adults ≥18 years with moderately to severely active UC (modified Mayo score 5–9, Mayo endoscopic subscore [MES] ≥2, and rectal bleeding subscore ≥1) with current or prior inadequate response or intolerance to corticosteroids, immunosuppressants, biologics, Janus kinase inhibitors, or sphingosine-1-phosphate receptor modulators, or a history of corticosteroid dependence.

Intervention: Participants were randomly assigned (1:1:1) to SC guselkumab 400 mg at weeks 0, 4, and 8 followed by 100 mg every 8 weeks (400/100 mg group); SC guselkumab 400 mg at weeks 0, 4, and 8 followed by 200 mg every 4 weeks (400/200 mg group); or matched placebo. Participants meeting rescue criteria at week 16 received guselkumab 400 mg at weeks 16, 20, and 24 followed by 100 mg every 8 weeks, while guselkumab-treated participants underwent sham rescue.

Outcomes: The primary outcome was clinical remission at week 12, defined as stool frequency subscore of 0 or 1 (not increased from baseline), rectal bleeding subscore of 0, and MES of 0 or 1 with no friability. Secondary outcomes included clinical remission at week 24, endoscopic improvement, histologic-endoscopic mucosal improvement, symptomatic remission, and safety.

Data Analysis: Efficacy analyses were conducted in the modified intention-to-treat population (all randomized participants who received at least 1 dose of study drug). Adjusted treatment differences between pooled guselkumab groups and placebo were estimated using a Cochran–Mantel–Haenszel method stratified by prior advanced therapy failure and baseline MES.

Funding: Johnson & Johnson (Janssen Research and Development).

Results: Between September 2022 and April 2024, 418 participants were randomized: 139 to the 400/100 mg group, 140 to the 400/200 mg group, and 139 to placebo. Mean age was 41.7 years, 61% were men, mean disease duration was 7.6 years, and mean modified Mayo score was 6.7.

At week 12, guselkumab achieved significantly higher rates of all primary and secondary endpoints compared to placebo, including clinical remission (28% vs 6%; adjusted difference 21 percentage points; *P* <0.001), clinical response (66% vs 35%; *P* <0.001), symptomatic remission (51% vs 21%; *P* <0.001), endoscopic improvement (37% vs 13%; *P* <0.001), and histologic-endoscopic mucosal improvement (31% vs 11%; *P* <0.001). Efficacy was consistent across advanced therapy–naïve and advanced therapy–experienced subgroups.

At week 48, among advanced therapy–naïve participants, clinical remission rates were 50.6% and 48.1% in the 400/200 and 400/100 mg groups, respectively, compared to 7.6% with placebo; among advanced therapy–experienced participants, rates were 32.7%, 21.1%, and 7.1%, respectively.

Adverse event rates were comparable between guselkumab and placebo groups, with no treatment-related deaths and no new safety signals identified through 48 weeks.

COMMENTARY

Why Is This Important?

Guselkumab was approved by the FDA in September 2024 for intravenous (IV) induction in UC. The subsequent approval of subcutaneous induction in September 2025, supported by the phase 3 ASTRO trial, represents an important shift in the IL-23 inhibitor landscape. While risankizumab and mirikizumab currently require IV induction for UC, guselkumab is now the first in its class to offer a fully subcutaneous induction and maintenance option.

For clinicians, ASTRO provides the data needed to determine which patients may reasonably avoid infusion-based therapy and begin treatment entirely at home.

Key Study Findings

ASTRO was a phase 3, randomized, placebo-controlled trial of 418 patients with moderate-to-severe UC. Patients received subcutaneous guselkumab 400 mg in weeks 0, 4, and 8, followed by maintenance dosing. The higher induction dose reflects the lower (~50%) bioavailability of subcutaneous administration compared to IV.

At week 12, the primary endpoint of clinical remission was achieved in 28% of patients receiving guselkumab compared to 6% with placebo (P <0.0001). Secondary endpoints, including clinical response and endoscopic improvement, were also significantly improved. Symptomatic improvement in stool frequency and rectal bleeding was observed as early as week 2–4, an important consideration for patients with active disease.

By week 24, clinical remission rates were maintained at approximately 35%–36%. Approximately 40% of participants had prior exposure to biologics, Janus kinase inhibitors, or sphingosine-1-phosphate modulators. Efficacy in this treatment-experienced population was consistent with the overall cohort, supporting use in later-line settings.

Caution

While the 28% remission rate at week 12 is numerically similar to IV induction data from the QUASAR trial[1], no direct head-to-head comparison exists. The inverse probability weighting analysis performed by the authors suggests comparable efficacy between SC and IV induction, but this remains indirect and hypothesis-generating.

Additionally, 56% of participants had severe endoscopic disease (Mayo endoscopic subscore 3) at baseline, which may limit generalizability to patients with milder disease.

The treat-through design further complicates interpretation of longer-term outcomes. At week 16, placebo non-responders were rescued with active therapy, which limits the strength of placebo comparisons at later time points.

Finally, the study was industry-funded, which should be acknowledged, although the trial design was rigorous.

Our Practice

In our practice, ASTRO does not make subcutaneous induction the default for all patients, but it clearly establishes it as a viable option.

We are most likely to prioritize a fully subcutaneous approach in patients with logistical barriers to infusion centers, including long travel distances or inflexible work schedules, as well as in those who strongly prefer self-administered therapy.

At the same time, we still consider IV induction in select situations. For patients with more severe disease, particularly those who were recently hospitalized or have markedly elevated inflammatory markers, we may favor IV induction to ensure immediate and reliable drug exposure, recognizing that direct comparative data are lacking.

More broadly, ASTRO reinforces the importance of not only selecting the appropriate therapeutic agent but also individualizing the delivery strategy to align with each patient's clinical needs and preferences.

Future Research

A key unanswered question is whether subcutaneous and intravenous induction strategies are truly equivalent in higher-risk populations. A prospective head-to-head trial would be particularly valuable.

In addition, as more IL-23 inhibitors and subcutaneous options become available, understanding the cost-effectiveness of avoiding infusion-related care will be increasingly important for both clinicians and health systems.

Conflict of Interest

The authors of the summary declare no conflicts of interest.

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Colonoscopy and FIT Shift CRC Detection Toward Earlier Stages: Results from the SCREESCO Trial


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This summary reviews Westerberg M, Ludvigsson, JF, Metcalfe C, et al. Colonoscopy and fecal immunochemical testing versus usual care in diagnostic colorectal cancer screening: the SCREESCO randomized controlled trial. Nat Med. 2026; 32: 1278-128

Correspondence to Romy Chamoun, MD. Associate Editor. Email: EBGI@gi.org

Keywords: Colonoscopy, colorectal cancer screening, fecal immunochemical testing

STRUCTURED ABSTRACT

Question: Does colorectal cancer (CRC) screening with primary colonoscopy or fecal immunochemical testing (FIT) improve early cancer detection compared with usual care, and what are the associated harms?

Design: This study is a randomized controlled trial (RCT) applying a randomized controlled block method.

Setting: The study was set across eighteen Swedish regions without established organized CRC screening programs.

Patients: The patients in the trial were 278,051 average-risk individuals aged 60 years randomized to colonoscopy, FIT, or usual care. The median follow-up was 4.8 years.

Intervention/Exposure: Participants were randomized to once-only screening

colonoscopy, 2 rounds of 2-stool FIT performed 2 years apart using a low positivity threshold (10 µg hemoglobin/g feces), and usual care without organized screening.

Outcomes: The outcomes patients faced were CRC incidence, CRC stage at diagnosis, gastrointestinal adverse events, cardiovascular adverse events, and all-cause mortality.

Data Analysis: Intention-to-screen analysis using incidence rate ratios comparing intervention groups with controls.

Funding: Supported by Swedish governmental and research funding agencies.

Results: Compared to usual care, both screening strategies resulted in a shift toward earlier-stage CRC diagnosis (**Table 1**).

Outcome	Colonoscopy vs Control	FIT vs Control
Any CRC	1.08 (0.91–1.28)	0.92 (0.81–1.05)
Stage I–II CRC	1.38 (1.09–1.74)	1.19 (0.99–1.43)
Stage III–IV CRC	0.86 (0.67–1.11)	0.71 (0.58–0.86)

Table 1. Rates of gastrointestinal and cardiovascular events were modestly increased during the first year after screening but became similar to controls over time. All-cause mortality did not differ between groups.

COMMENTARY

Why Is This Important?

CRC screening is one of the most successful cancer prevention strategies, reducing both CRC incidence through adenoma removal and CRC mortality through earlier cancer detection. Colonoscopy and FIT are the 2 most widely used screening modalities and are recommended by multiple professional societies. However, few contemporary randomized trials have compared these screening approaches against an unscreened population, making it difficult to quantify the overall benefits and harms attributable to screening itself.

The SCREESCO trial addresses this important knowledge gap by comparing colonoscopy-based screening, FIT-based screening, and usual care in a large average-risk population. Unlike studies that focus solely on CRC mortality, SCREESCO provides insight into what occurs during the diagnostic phase of screening, including cancer detection, stage distribution, and procedure-related adverse events. Understanding these early outcomes is important because a shift toward detection of stage I–II cancers and away from advanced-stage disease is often the first measurable indicator that a screening program may ultimately improve long-term CRC outcomes.

As healthcare systems continue to expand organized CRC screening programs and seek strategies that maximize participation, the results of SCREESCO provide valuable evidence supporting both colonoscopy and FIT as effective screening approaches. These findings help inform discussions between providers, patients, and policymakers regarding the implementation of population-based CRC screening programs and the balance between screening benefits and associated risks.

Key Study Findings

More stage I-II CRCs detected with screening suggests earlier diagnosis and opportunity for curative treatment. Fewer advanced CRCs were observed, especially with FIT indicating a favorable stage shift. It was found that serious adverse events were uncommon, which supports the safety of organized screening. There is no mortality difference observed yet, but the follow-ups remain ongoing. Both colonoscopy and FIT demonstrated benefits compared with usual care, which supports the continued expansion of CRC screening programs.

Caution

SCREESCO reports early outcomes from the diagnostic phase of screening rather than the long-term outcomes that matter most to patients, including CRC incidence and CRC mortality. This analysis represents the diagnostic phase of screening with a median follow-up of 4.8 years and was not designed to assess the effect of screening on CRC mortality. While the observed shift toward earlier-stage disease is encouraging, additional follow-up is needed to determine whether these findings translate into meaningful reductions in CRC-related deaths. Participation rates were lower than anticipated, particularly in the colonoscopy arm, which may attenuate the benefits observed in this intention-to-screen analysis. Longer follow-ups through 2030 are planned.

Our Practice

In our practice, we begin CRC screening starting at age 45 years for patients assessed to be at average risk for CRC. The decision to continue or stop screening after age 75 years is individualized. All screening options are reviewed with patients, including colonoscopy, stool tests, blood tests, and imaging.

No current screening modality has 100% sensitivity for CRC detection. While colonoscopy and stool-based tests are both considered first line screening modalities for CRC, that does not make them equivalent. We specifically address the difference in sensitivity in detecting pre-cancerous polyps. While colonoscopy is considered to be 90-95% sensitive for detection of advanced colon polyps, FIT testing is ~25% sensitive, and multitarget stool DNA testing (mt-sDNA) is ~45% sensitive. We simplify this for patients by saying that colonoscopy will capture the majority of these lesions while stool and blood tests will miss more than half.

When a patient opts for stool-based testing, we emphasize the differences between FIT and mt-SDNA. FIT is readily available at the lab in our clinic, meaning patients can complete the test on the same day or at least pick up a stool collection kit on the same day and later submit the test to our lab or to many nearby labs which may be closer to where they live. Only a small stool sample is required for the test. A mt-sDNA is a send-out test and requires collection of a full bowel movement, which may be perceived as additional barriers in some patients. Advantages of mt-sDNA include potentially higher sensitivity for both CRC and precancerous colon polyps and only needing to perform the test every 3 years (vs annually for FIT). Conversely, mt-sDNA may have a higher false-positive rate (decreased specificity) as compared to FIT, potentially leading to more downstream colonoscopies for patients who may have been hoping to avoid colonoscopy in the first place.

For patients and providers trying to understand the benefits and risks of CRC screening via colonoscopy or FIT, the SCREESCO study provides valuable data we can share with our patients to help them make informed decisions. An important caveat in extrapolating the FIT data from this study to patients in the United States is to highlight that while the SCREESCO trial used a two-stool FIT protocol, we typically perform annual single-sample testing in the United States.

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Future Research

Future studies should evaluate whether intervention strategies that target low-value surveillance colonoscopy can be implemented without compromising patient outcomes. Research is also needed to identify barriers to guideline adherence among endoscopists and patients, assess the effectiveness of decision-support tools integrated into electronic health records, and determine whether personalized surveillance recommendations based on individual risk factors can further optimize colonoscopy utilization while maintaining colorectal cancer prevention benefits.

Conflict of Interest

The authors report no relevant conflicts of interest related to this commentary.

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AI-Assisted Endoscopy: Can AI Change Gastric Cancer Detection?

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This summary reviews Dong Z, Wu L, Du H, et al. Effect of a computer-aided device for detecting gastric neoplasms: a multicenter, randomized controlled trial. Gastroenterology. 2026; 170(7): 1518-1532.

Correspondence to Margaret J. Zhou, MD, MSc. Associate Editor. Email: EBGI@gi.org

Keywords: Artificial intelligence, gastric cancer, gastric neoplasms, endoscopy

STRUCTURED ABSTRACT

Question: Does artificial intelligence (AI)-assisted computer-aided detection during esophagogastroduodenoscopy (EGD) improve the detection rate of gastric neoplasms compared with standard EGD?

Design: This is a multicenter, single-blind open-label, parallel-group, randomized controlled trial (RCT) with 1:1 allocation.

Setting: It was set across 24 hospitals in China with enrollment from December 21, 2021, to November 11, 2023.

Patients: The patients were adults ≥18 years undergoing sedated EGD for screening, surveillance, or evaluation of upper gastrointestinal (GI) symptoms. Participating endoscopists were required to perform at least 500 EGDs and complete a training module with at least 10 AI-assisted exams.

Intervention: Patients were randomized to AI-assisted EGD (using the ENDOANGEL-GN system) or standard non-assisted EGD. The AI system, built

on deep convolutional neural networks, provided real-time anatomic landmark identification and blind spot monitoring during the procedure as well as lesion detection with risk stratification. Detected lesions are demarcated by a blue box, and if the lesion is predicted to be high-risk for neoplasia, the box turns red, and if low-risk the box stays blue (**Figure 1**).[1] Use of image-enhanced modalities and decisions about taking biopsies for lesions detected with a blue box were decided at the discretion of the endoscopist. Lesions highlighted with a red box required biopsy.

Outcomes: The primary outcome was the detection rate of gastric neoplasms after centralized endoscopic and pathologic review. Secondary outcomes included: 1) detection rate of gastric neoplasms based on original clinical pathology (before centralized pathologic review); 2) relative early gastric cancer (EGC) detection ratio with or without centralized pathology review; 3) detection rate of intestinal metaplasia (IM) or gastric atrophy before or after pathologic review; 4) biopsy rate; 5) procedure time; 6) inspection time; and 7) number of blind spots. EGC was defined as cancer limited to the mucosa or submucosa with or without regional lymph node metastasis (including high-grade intraepithelial neoplasia [HGIN]).

Original pathology is defined as the initial pathologic diagnosis provided by each center before centralized review. Centralized endoscopic and pathologic review occurred for all gastric neoplasms and non-neoplastic lesions that had suspicious features on endoscopy.

Expert panels consisted of endoscopists with >10 years of experience and pathologists with >15 years of experience. Expert pathologists were blinded to the initial pathologic diagnosis. Both panels were blinded to lesion randomization status. For lesions that underwent centralized review, the final diagnosis required agreement from ≥1 expert pathologist for preliminary neoplastic diagnosis, and agreement from ≥2 expert pathologists for preliminary non-neoplastic diagnosis to reclassify to neoplastic.

Data Analysis: Intention-to-treat (ITT), per-protocol (PP), and exploratory subgroup analyses were performed. Risk ratios (RR) with 95% confidence intervals (CI) were reported.

Funding: National Key Research and Development Program of China, Natural Science Foundation of Wuhan, Key Research and Development Program of Hubei Province, College-enterprise Deepening Reform Project of Wuhan University, National Natural Science Foundation of China-Youth Science Fund

Results: In the ITT analysis, 29,514 patients were included and 26,001 were included in the PP analysis. Some patients were excluded from the PP analysis due to uncertainty about group allocation and deviations from the protocol. Some endoscopists in the control group activated the AI function to evaluate lesions.

The primary outcome of the study was that AI did not significantly improve the detection rate of gastric neoplasms after centralized pathologic review (1.42% vs 1.25%; RR 1.13, 95% CI 0.92–1.38; $P = 0.25$) in the ITT analysis.

The secondary outcomes were that, based on original pathology (before expert review), AI-assisted EGD showed a statistically significantly higher rate of detection of gastric neoplasms (4.06% vs 3.57%; RR 1.14, 95% CI 1.0–1.28; $P = 0.03$). Comparing EGD with versus AI assistance, relative EGC detection ratio was similar (RR, 1.06; 95% CI, 0.62-1.81; 41.46% vs 39.05%; $P = 0.81$) and detection of IM or gastric atrophy was similar (2,703 of 14,767 [18.30%] vs 2650 of 14,747 [17.97%]; $P = 0.46$). Rate of biopsy was also comparable (54% vs 53%; $P = 0.20$). Similar findings were seen in the PP and ITT analyses.

AI reduced the mean number of blind spots from 2.52 to 1.07 ($P < 0.001$), and AI prolonged both procedure and inspection time (procedure time with AI 7.69 vs without AI 7.33 min; $P < 0.001$; inspection time with AI 7.35 min vs 6.99 min; $P < 0.001$).

Among endoscopists with <3 years experience, there was a statistically significant higher detection rate of gastric neoplasms with AI (1.44% vs 0.78%; RR, 1.83; 95% CI, 1.04–3.21). In the PP analysis, RR of neoplasm detection was higher when endoscopists were in the fatigue period than at the nonfatigue period (RR 1.60, 1.07–2.40 vs 1.03, 0.80–1.33, P for interaction =0.07).

In the experimental group, AI correctly identified 100% of pathologically confirmed gastric adenocarcinomas, 91.9% of high-grade intraepithelial neoplasia, and 57.1% of low-grade intraepithelial neoplasia.

COMMENTARY

Why Is This Important?

This is the largest RCT to date on AI-assisted gastric neoplasm detection and provides critical real-world evidence on the impact of AI-assisted EGD. Prior retrospective and smaller prospective studies demonstrated high accuracy of AI for upper GI neoplasia detection, but robust multicenter RCT evidence was lacking. A recent meta-analysis of 11 RCTs (57,512 participants) found that AI-assisted EGD improved any upper GI neoplasm detection overall (RR 1.57, 95% CI 1.23–2.01).[2] While there was significantly increased detection for lesions ≤10 mm (RR, 2.24; 95% CI, 1.72-2.91), detection rate for lesions >10 mm was similar. Another recent meta-analysis of 26 studies (43,088 patients) found that AI-assisted EGD achieved a sensitivity of 90%, specificity of 92%, and AUC of 0.96 for early gastric cancer detection, significantly outperforming clinician-level performance (AUC 0.85–0.90).[3] Existing literature seems to suggest a potential benefit of AI-assisted EGD for upper GI neoplasm detection. However, the significant discrepancy seen in the impact of AI-assisted EGD using central pathology review versus not in this trial does call into question whether pathology review may significantly impact any detected differences seen with AI assistance. Most AI studies on this question have not required centralized pathology review, and this study importantly raises the question of whether this should be included for training AI models moving forward.

This trial also offers additional support to potential use of AI-assisted EGD to improve endoscopic quality. The miss rate for early gastric cancer is around 10%, and higher among inexperienced endoscopists, in part due to subtle features of early lesions.[4] One mechanism for this is likely the reduction in blind spots seen with AI. This trial builds on prior evidence studying the ENDOANGEL system that showed that the AI group has fewer blind spots compared to conventional EGD (mean 5.4 vs 9.8, *P* <0.001).[5] A prior RCT using the ENDOANGEL system at a single-center tandem trial of 1,812 patients found that AI significantly reduced the miss rate of gastric neoplasms (RR 0.224, 95% CI 0.068–0.744), with particular benefit for lesions ≤10 mm.[6]

Key Study Findings

AI-assisted EGD did not significantly improve gastric neoplasm detection after centralized pathologic review. Of note, the original diagnosis of 84% (804 of 962) low-grade intraepithelial neoplasia and 14% (7 of 50) HGIN were downgraded to benign lesions after the centralized pathology review, while only 0.72% (6/837) of non-neoplastic lesions were upgraded to neoplasms. This accounted for a substantial difference in the rate of gastric neoplasms that was reported for results based on preliminary review versus centralized pathology review. Interestingly, AI did improve detection based on original pathology.

Detection of EGC or IM/gastric atrophy was similar with vs without AI assistance based on both preliminary and centralized review pathology. AI significantly reduced endoscopic blind spots (from 2.52 to 1.07, *P* <0.001), supporting its value as a quality assurance tool for mucosal inspection completeness, consistent with earlier ENDOANGEL trials. The subgroup analysis showing greater benefit of the AI system among less experienced endoscopists and more fatigued operators suggests AI may be most impactful in settings where baseline endoscopy quality may be suboptimal.

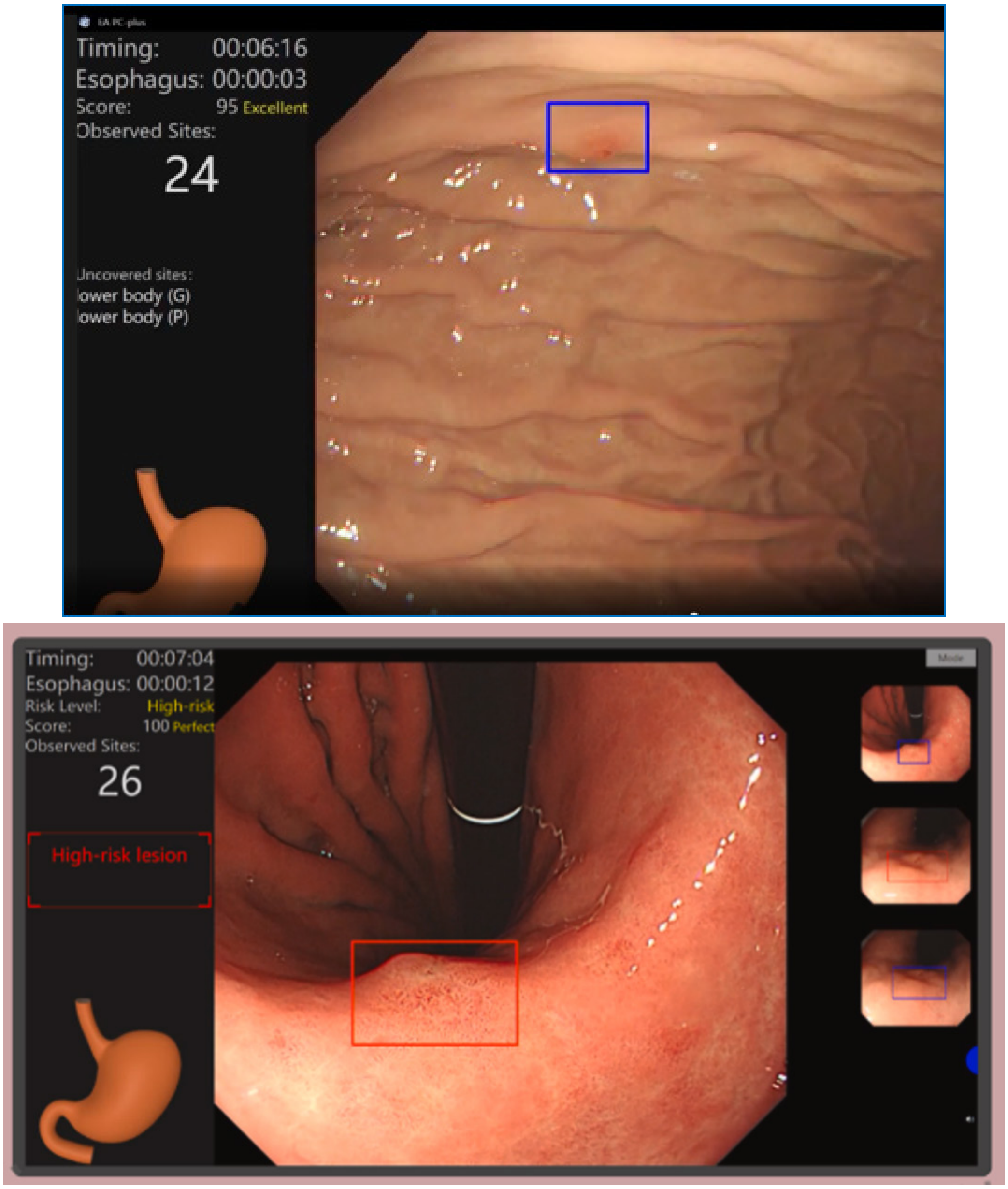

Figure 1. Top: Blue bounding box demarcates a low-risk lesion detected by the ENDOANGEL-GN system. Bottom: Red bounding box demarcates a high-risk lesion detected by the ENDOANGEL-GN system.

Caution

This trial was conducted in China, a region with high gastric cancer prevalence and where endoscopists are generally more experienced in gastric evaluation, and the majority of procedures were performed at tertiary hospitals or by senior endoscopists. This may limit generalizability to lower-prevalence settings or endoscopists with less experience with diagnosis of gastric neoplasms. The study authors also highlight the high quality of EGD performed in the control group in this study, with mean procedure time in the control group of 7.3 minutes and only 2.5 blind spots in the control group. The authors explored neoplasm detection rates among AI-exposed vs AI-naïve endoscopists and found higher detection rates among AI-exposed endoscopists, which may suggest a possible training bias among those with AI exposure. Further study of downstream effects of AI exposure should be conducted to explore this.

My Practice

This trial tempers enthusiasm for immediate widespread adoption of AI-assisted EGD as a tool to improve gastric neoplasm detection rates in high-volume, experienced endoscopy settings. However, the significant reduction in blind spots supports the use of AI as a quality monitoring tool during EGD. In practice, AI may be most valuable for improving gastric neoplasm detection in lower-volume settings with endoscopists less experienced with neoplasm detection, when operator fatigue may be a concern, and as an endoscopic training tool.

Future Research

Future trials should evaluate AI performance in less experienced endoscopy units to evaluate use in more generalizable real-world settings, as well as stratified b y endoscopist experience level. Future studies should also incorporate advanced imaging modalities, like narrow-band imaging and linked color imaging, with AI.

Conflict of Interest

Dr. Zhou reports no relevant conflicts of interest.

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EVIDENCE-BASED GI
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Beyond Graft Survival: A Practical Guide to Long-Term Care After Liver Transplantation


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This summary reviews Sharma P, Izzy M, Ghabril MS, et al. AASLD AST Practice Guideline on adult liver transplantation: Diagnosis and post-transplant management of non-graft–related complications. Liver Transplantation. 2026. doi: 10.1097/LVT.0000000000000785. Epub ahead of print.

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Keywords: Liver transplantation, non-graft complications, metabolic syndrome, chronic kidney disease, immunosuppression

LIVER

STRUCTURED ABSTRACT

Question: What are the best practices for preventing and managing non-graft-related complications in adult liver transplant (LT) recipients beyond the first 90 days post-transplant?

Design: Multidisciplinary practice guideline developed jointly by American Association for the Study of Liver Disease (AASLD) and American Society of Trasplantation (AST). Clinical questions were structured in PICO format. A systematic literature search was conducted through Ovid MEDLINE and Embase (January 2016 to May 2023), supplemented by an updated search in December 2024. Recommendations were graded using the Oxford Center for Evidence-Based Medicine framework and classified as strong or weak based on evidence quality, risk-benefit ratio, and patient preferences. Consensus required at least 80% agreement among panel members.

Setting: All clinical settings where adult liver transplant recipients are followed beyond the early postoperative period, including transplant centers and primary care practices.

Patients: Adult liver transplant recipients more than 90 days post-transplant with non-graft-related comorbidities including metabolic, cardiovascular, renal, oncologic, infectious, and musculoskeletal complications.

Intervention/Exposure: Key recommendations include

- Annual screening for hypertension, diabetes, obesity, and dyslipidemia in all recipients; early corticosteroid withdrawal in those with metabolic comorbidities.

- Glucagon-like peptide-1(GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors as first-line therapy for diabetic recipients at high cardiovascular or renal risk; metformin for those without such risk factors.

- Hydrophilic statins as first-line therapy for dyslipidemia; amlodipine or felodipine as preferred antihypertensives in recipients without cardiovascular or renal comorbidities.

- Calcineurin inhibitors (CNI) minimization combined with mycophenolate or everolimus within the first year for chronic kidney disease (CKD); beyond 1 year, in CKD patients, CNIs should be minimized but not eliminated.

- Pre-emptive weekly cytomegalovirus (CMV) monitoring with polymerase chain reaction (PCR) testing for 100 days is preferred if either the recipient or donor is CMV+; if this cannot be performed, then Valganciclovir 900 mg daily (or renally dosed) for 3 months (D±/R+) or 6 months (D+/R-) is advised.

- *Pneumocystis jiroveci* pneumonia prophylaxis is recommended for 6 months post-transplant with trimethoprim-sulfamethoxazole or atovaquone.

- Annual total full-body skin examination, given that the most common post-LT cancer is non-melanoma skin cancer.

- Colonoscopy is the preferred modality for colon cancer screening. Screening cadence follows the general population but may consider every 5 years.

- Dual-energy x-ray absorptiometry (DXA) at 6 months post-transplant; pharmacologic therapy for T-score ≤ -2.5 or fracture risk assessment tool (FRAX) $\geq 20\%$ for major fracture risk.

- Delay pregnancy until 1-year post-transplant and with at least 6 months of graft stability. Mycophenolic acid products should be discontinued at least 6 weeks before conception in women and 90 days in men.

Calcineurin inhibitors, azathioprine and steroids are safe in pregnancy.

Outcomes: Patient survival, graft survival, cardiovascular events, renal function, de novo malignancy incidence, infection-related mortality, and quality of life.

Data Analysis: Recommendations were graded strong or weak using the Oxford Center for Evidence-Based Medicine framework. The recommendations are derived from retrospective cohort studies, systematic reviews, and extrapolations from the general population, reflecting a persistent evidence gap in prospective transplant-specific data.

Funding: Funded by the AASLD. No external or industry funding was utilized.

Results: The guideline provides 87 recommendations across 9 clinical domains. Long-term mortality after LT is driven predominantly by complications of immunosuppression, recurrent disease, and medical comorbidities rather than graft failure. Highlights are presented below, with key recommendations summarized (**Table 1**) and the temporal trajectory of post-transplant infections illustrated (**Figure 1**).

Rates of gastrointestinal and cardiovascular events were modestly increased during the first year after screening but became similar to controls over time. All-cause mortality did not differ between groups.

Metabolic syndrome affects more than half of LT recipients, with de novo incidence of 24.7% (95% CI 18% to 32.9%) over 15 months post-transplant.[1] Hypertension is present in 53 to 62%, dyslipidemia in 30 to 71%, diabetes in 25 to 40%, and obesity in 36 to 41% of recipients.[2] Early corticosteroid withdrawal within the first 2 months significantly reduces post-transplant diabetes and hypertension, supported by a Cochrane review of 17 randomized trials, with only a modest increase in rejection risk.[3] GLP-1 receptor agonists and SGLT-2 inhibitors are recommended as first-line agents in high-risk recipients, with referral to obesity specialists suggested as early as 3 to 6 months post-transplant in those with a body mass index above 30.[4] Hydrophilic statins (e.g. pravastatin or rosuvastatin) are preferred for dyslipidemia given their favorable CYP3A4 profile and minimal interaction with CNIs.[5] In recipients without cardiovascular or renal comorbidities, amlodipine or felodipine are the preferred first-line antihypertensive agents given the mechanism of reversal of CNI-induced renal vasoconstriction.

LT recipients have the highest risk of incident advanced CKD, with early end-stage renal disease rates rising from 21.8 to 36.3 per 1,000 patient-years between the pre-model for end-stage renal disease and end-stage renal disease eras.[6] CNI reduction combined with mycophenolate or everolimus within the first year is strongly recommended. The landmark H2304 trial demonstrated sustained estimated glomerular filtration rate improvement with everolimus plus reduced tacrolimus through 36 months with comparable rejection rates.[7] The EVEROLIVER registry confirmed that early conversion within 3 months allowed 55% of patients with baseline estimated glomerular filtration rate below 60 mL/min/1.73 m² to recover above that threshold at month 36, with no benefit observed in those converted after 12 months.[8] Use of Belatacept and discontinuation of calcineurin inhibitors in the early postoperative period is not recommended due to high rates of graft failure.[9]

Infection timing follows a well-described trajectory: nosocomial and donor-derived infections predominate in the first month, opportunistic infections from months 1-12, and community-acquired infections thereafter (**Figure 1**). In a randomized trial of 205 CMV D+/R recipients, CMV disease incidence was significantly lower with pre-emptive weekly PCR monitoring than with universal valganciclovir prophylaxis (9% vs 19%, P=0.04), with superior CMV-specific immune reconstitution in the pre-emptive arm.[10] In refractory or resistant cases with low levels of viremia (≤20,000 IU/mL), Maribavir 400 mg twice daily is preferred, supported by a phase 3 randomized trial.[11]

LT recipients carry a 2.45-fold increased overall cancer risk compared with the general population.[12] While non-Hodgkin lymphoma carries the highest standardized incidence ratio, non-melanoma skin cancer is the most common, yet annual skin exams remain inconsistently performed. For colon cancer screening, colonoscopy is preferred over stool-based testing given an adjusted odds ratio of 2.38 (95% CI 1.07 to 5.3) for advanced adenomas in solid organ transplant recipients.[13] Serial Epstein-Barr virus PCR for post-transplant lymphoproliferative disorder screening is not supported.[14]

Post-transplant osteopenia, osteoporosis, and fractures are reported in 35%, 12%, and 20% of recipients respectively, with an incidence of 11% for vertebral fractures.[15] DXA at 6 months post-transplant and every 1 to 2 years in those with baseline abnormalities is strongly recommended. Pharmacologic therapy is indicated for T-scores ≤−2.5 or FRAX ≥20%.

Pregnancy within 12 months of transplant is associated with significantly lower live birth rates (80% vs 98%) and higher rates of rejection (46% vs 11%) compared with after 12 months.[16] Mycophenolic acid is contraindicated in pregnancy and should be discontinued at least 6 weeks before conception in women and 90 days in men.[17]

COMMENTARY

Why Is This Important?

Scientific Registry of Transplant Recipients data demonstrate excellent long-term outcomes after liver transplantation with 5- and 10-year survival approaching 82% and 69%, respectively. As graft survival continues to improve, the major threats to long-term survival shifted from graft failure to cardiovascular disease, malignancy, renal failure, and infection. Despite this transition, management of non-graft complications remains highly variable across transplant centers and primary care settings. This guideline provides the first comprehensive, evidence-based framework for long-term management of adult liver transplant recipients. Importantly, many recommendations address conditions commonly managed outside transplant centers, emphasizing the critical role of coordinated care between transplant hepatologists, primary care physicians, and other specialists.

Key Study Findings

One of the most notable observations is the unexpectedly high burden of CKD among liver transplant recipients. The EVEROLIVER registry makes a compelling case for early reduction in calcineurin inhibitors and conversion to mTOR inhibitors, while conversion after 12 months provided no benefit.[8] These data suggest a narrow therapeutic window during which renal recovery remains achievable.

The introduction of GLP-1 receptor agonists has offered a paradigm shift for therapeutic options for post-LT patients with diabetes mellitus or obesity. Additional favorable properties include their renal protective and anti-inflammatory effects. Adjusting immunosuppression while on a GLP-1 receptor agonist is not needed.[4]

Regarding post-LT malignancy, non-melanoma skin cancer is the most common, yet annual skin exams remain one of the most inconsistently performed interventions in this population. The preference for colonoscopy over stool-based testing and consideration of every 5-year surveillance should be acknowledged.[13]

The reproductive data are among the most actionable in the guideline. An 18-percentage-point difference in live birth rates and a 35-percentage-point difference in rejection rates based solely on timing of conception suggest that family planning is an integral part of every pre-transplant and post-transplant conversation.[16]

Caution

Several strong recommendations, including annual metabolic screening, are based on level 5 evidence reflecting expert consensus rather than robust data. Equity considerations are minimally

Domain	Key Recommendation	Strength/Level
Metabolic screening	Annual screening for hypertension, diabetes, obesity, and dyslipidemia in all recipients	Strong, Level 5
Corticosteroids	Early withdrawal within 2 months in recipients with diabetes mellitus or hypertension	Strong, Level 1
Diabetes, no CV/renal risk	Metformin is first-line	Strong, Level 5
Diabetes, high CV or renal risk	GLP-1 receptor agonists and/or SGLT-2 inhibitors are first-line	Strong, Level 5
Obesity (BMI >30kg/m2)	Referral to obesity specialist at 3–6 months; GLP-1 RA if diet and exercise insufficient	Strong, Level 3–5
Hypertension, no CV/CKD	Amlodipine or felodipine are first-line	Strong, Level 5
Hypertension, with CV disease or CKD	RAS inhibitors are first-line	Strong, Level 5
Dyslipidemia	Hydrophilic statins are first-line; consider ezetimibe or PCSK9 inhibitors for refractory cases	Strong, Level 5
CKD, immunosuppression	CNI reduction combined with mycophenolate or everolimus within the first year; thereafter, CNIs minimized but not eliminated	Strong, Level 1
CKD, belatacept	Contraindicated due to increased mortality risk	Strong, Level 1
CKD surveillance	Creatinine-based estimated glomerular filtration rate every 6–12 months (stages 1–3); every 1–3 months (stages 4–5)	Strong, Level 4
CMV prophylaxis, preferred strategy	Pre-emptive weekly CMV PCR for 100 days when feasible	Strong, Level 1
CMV prophylaxis, alternative	Valganciclovir prophylaxis (3 months D±/R+; 6 months D+/R−)	Strong, Level 1
CMV, refractory or resistant	Maribavir 400 mg BID (viral load ≤20,000 IU/mL); IV foscarnet for high viral load or severe disease	Strong, Level 1
Pneumocystis jiroveci pneumonia prophlaxis	Trimethoprim-sulfamethoxazole or atovaquone for 6 months	Strong, Level 2

Domain	Key Recommendation	Strength/Level
Candida prophylaxis	Risk-based assessment; fluconazole 2-4 weeks	Strong, Level 2
Post-transplant lymphoproliferative disorder screening	Serial assessment of Epstein-Barr virus PCR is not advised	Weak, Level 3
Skin cancer	Annual full-body skin examination	Strong, Level 2
Colorectal cancer	Colonoscopy preferred over stool-based testing; consider every 5 years in average-risk recipients ≥45 years	Weak, Level 3
Colorectal cancer, IBD with or without PSC	Annual colonoscopy with random biopsies	Strong, Level 1–2
Colorectal cancer, PSC without IBD	Colonoscopy every 5 years with biopsies	Strong, Level 3
Bone health	DXA at 6 months post-transplant; pharmacotherapy for T-score ≤−2.5 or FRAX ≥20%	Strong, Level 1–2
Pregnancy timing	Delay pregnancy ≥12 months post-transplant	Strong, Level 3
Pregnancy, immunosuppression	Discontinue MPA ≥6 weeks before conception in women; ≥90 days in men	Strong, Level 1

Table 1. Key recommendations from the AASLD/AST Practice Guideline on non-graft–related complications after adult liver transplantation.
BID, twice a day; BMI, body mass index; CKD, chronic kidney disease; CMV, cytomegalovirus; CNI, calcineurin inhibitor; CV, cardiovascular; DXA, dual-energy x-ray absorptiometry;GLP-1, glucagon-like peptide-1; IBD, inflammatory bowel disease; FRAX, fracture risk assessment tool; MPA, mycophenolic acid PCR, polymerase chain reaction; PSC, primary sclerosing cholangitis; RAS, renin–angiotensin system; SGLT2, sodium-glucose cotransporter-2.

addressed: differential access to GLP-1 receptor agonists and subspecialists across socioeconomic and geographic strata, an omission that implementation-focused readers should account for in local adaptation of these recommendations.

Our Practice

This guideline reinforces several aspects of my current practice while highlighting opportunities for earlier intervention. I routinely emphasize aggressive cardiovascular risk-factor modification after transplantation, but these recommendations support earlier incorporation of GLP-1 receptor agonists and SGLT-2 inhibitors in appropriate high-risk recipients. This point highlights the need for integration in a multi-disciplinary fashion with other specialists such as endocrinologists, dieticians, primary care providers, and pharmacists. In this manner, we are able to identify at risk patients earlier, though access to care

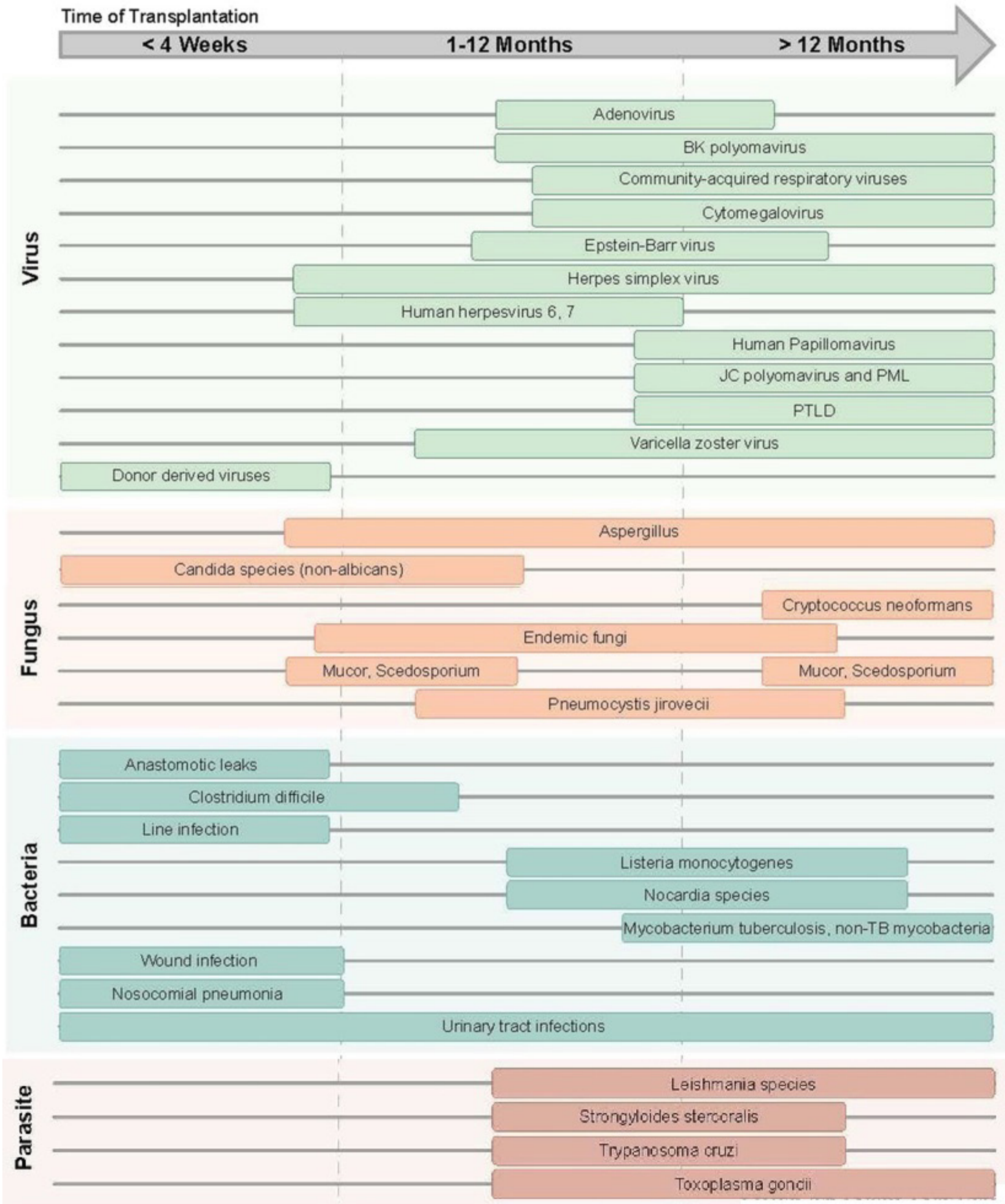

Figure 1. Timeline of common post-transplant infections. Time course of infection based upon time from the index liver transplant. PTLD, post-transplant lymphoproliferative disorder.

is often still limited by insurance barriers.

The data regarding early calcineurin inhibitor minimization are particularly compelling and reinforce the importance of recognizing chronic kidney disease before irreversible injury develops. Although we hope for renal recovery within the first year post-LT, we want to identify patients earlier before the window for safety net closes. Novel biomarkers for detecting early kidney dysfunction could aid risk stratification.

The guideline also serves as a reminder that cancer surveillance should remain a priority long after transplant follow-up intervals become less frequent. Annual dermatologic examinations and transplant-specific colorectal cancer surveillance are interventions that can easily be overlooked during long-term care. As graft function stabilizes with time, visits with my post-LT patients focus on well-being, including quality of life, sexual health, family planning, and mental health, among others. Providers can use dot phrases to ensure all aspects are addressed, and pre-visit surveys to screen for topics that patients may not traditionally feel comfortable discussing. It takes a village to help our patients get through transplant, and the same can be said post-transplant. Integral to the care of our patients is communicating with primary care providers to ensure that these post-transplant screening metrics are addressed.

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Future Research

Future research should prioritize prospective transplant-specific studies evaluating immunosuppression strategies, metabolic therapies including GLP-1 receptor agonists, and interventions that reduce cardiovascular risk after transplantation. Biomarkers to detect early chronic kidney disease and post-transplant lymphoproliferative disorder are needed. Equally important are implementation studies evaluating how transplant centers can improve adherence to cancer surveillance, bone health screening, and preventive care recommendations across diverse patient populations.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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EVIDENCE-BASED GI
AN ACG PUBLICATION

Patients With Advanced Adenomas on Index Exam are at Increased Risk for Metachronous Advanced Neoplasia at Second Surveillance

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This summary reviews Javidi DJ, Obaida D, Mackenzie TA, et al. Association between index adenomas and advanced findings at third colonoscopy: Data from the New Hampshire colonoscopy registry. Clin Gastroenterol Hepatol. 2026; Online ahead of print.

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Keywords: Colorectal cancer, surveillance colonoscopy, polyps

STRUCTURED ABSTRACT

Question: There is a paucity of data informing risk of metachronous advanced neoplasia at second surveillance colonoscopy. The objective of this study was to examine the risk for an advanced finding (large SP, advanced adenomas [AA], or colorectal cancer [CRC]) on second surveillance colonoscopy in individuals with advanced adenomas on index exam and a first surveillance colonoscopy without polyp findings, accounting for potential confounders including adenoma detection rate, smoking, body mass index (BMI), and family history of CRC.

Design: Retrospective analysis of data from the New Hampshire Colonoscopy Registry (NHCR) which is a prospective statewide colonoscopy registry.

Setting: Endoscopy centers across New Hampshire, USA.

Patients: To be included in the analysis, patients were required to have no previous neoplasia and 2 surveillance colonoscopies at least 12 months apart with a first surveillance colonoscopy without polyp findings. Patients who had any CRC,

advanced adenomas, tubular adenomas, large serrated polyps (≥ 1 cm), dysplastic sessile serrated polyps, traditional serrated adenomas, or any sessile serrated polyps on first surveillance exam were excluded.

Exposure: Individuals were stratified into 4 groups based on index exam findings: no adenomas, 1-2 non-advanced adenomas, 3-4 non-advanced adenomas, and advanced adenomas or 5+ non-advanced adenomas.

Outcomes: The primary outcome was detection of advanced neoplasia (advanced adenomas or CRC) on the second surveillance exam.

Data Analysis: The authors ran a Poisson model regression using robust standard errors which predicted advanced findings on second surveillance exam, adjusting for age, sex, family history of CRC, smoking, serrated polyps on index exam, BMI, and adenoma detection rates of index and first surveillance endoscopists with months to second follow-up exam as an offset variable.

Funding: Division of Cancer Prevention, National Cancer Institute, 5R01CA243449, Optimizing colorectal cancer prevention: a multi-disciplinary, population-based investigation of serrated polyps using risk prediction and modeling; and ACG 2023 clinical research grant.

Results: In the study, 3,171 patients were included and risk-stratified into 4 different groups based on index colonoscopy findings; no adenomas (n=1948), 1-2 non-advanced adenomas (n=846), 3-4 non-advanced adenomas (n=69) and, advanced adenomas or 5+ non-advanced adenomas (n=308).

Only those with advanced adenomas or 5+ non-advanced adenomas had a higher risk for metachronous advanced adenomas or CRC (RR=3.47 95% CI: 1.46-8.24).

COMMENTARY

Why Is This Important?

The investigators found that the risk for advanced outcomes in patients with AA or 5+ non advanced adenomas was increased at the second surveillance colonoscopy despite an interim first surveillance exam without polyps. This risk was modified by several factors, including the endoscopist's adenoma detection rate at the first surveillance, patient smoking status, and high-risk serrated polyps on the index exam. Specifically, smoking status evaluated at the initial surveillance was associated with a nearly threefold increase in risk for advanced findings on the second surveillance. While smoking is an established risk factor for advanced neoplasia, this is the first study to demonstrate its impact at the second surveillance interval.[1,2]

However, after adjusting for these covariates, this association was observed to be independent of adverse drug reaction and important risk factors such as smoking and BMI. These data support the US Multi-Society Task Force on Colorectal Cancer (USMSTF) recommendation of 5-year follow-up for these patients.[3] These data address the knowledge gap regarding the risk at second surveillance colonoscopies which were not addressed by previous studies.

Studies from the Netherlands and the VA have observed that high-risk conventional adenomas on an index colonoscopy increases the risk of significant lesions on a second surveillance, despite a clear first surveillance.[4,5] However, a recent meta-analysis highlighted critical limitations in these published data.[6] These limitations include failing to account for endoscopist performance (adenoma detection rate and bowel preparation quality) and patient risk factors such as smoking, BMI, genetic predispositions, and whether the baseline exam was conducted for surveillance.

The investigators addressed prior limitations by adjusting for quality measures and known CRC risk factors in patients who underwent 2 subsequent surveillance exams. The study cohort was restricted to patients with no polyps detected during their first surveillance. This is important since individuals with findings (e.g., advanced adenomas) are assigned rigorous surveillance intervals

Advanced adenoma or CRC on second surveillance colonoscopy		
No adenomas (N = 1,948)	N=39 (2.0%;1.5-2.7)	Rate ratio=1.0 (Reference)
1-2 non-advanced adenomas (N = 846)	N=36 (4.26%:3.1-5.8)	**1.84 (0.94 – 3.59)**
3-4 non-advanced adenomas (N = 69)	N=3 (4.4%:1.5-12.0)	**2.26 (0.48 - 10.67)**
AA/5+ non-advanced adenomas (N = 308)	N=17 (5.5%:3.5-8.6)	**3.47 (1.46 – 8.24)**

Table 1. Advanced neoplasia on second surveillance colonoscopy
* Results from a Poisson model regression which predicted advanced neoplasia on second surveillance exam, adjusting for age, sex, family history of CRC, smoking, serrated polyps on index exam, BMI, adenoma detection rates of index and first surveillance endoscopists with months to second follow-up exam as the offset variable.

regardless of their index exam. Thus, this is the first study to assess the risk of advanced outcomes on a second surveillance colonoscopy among patients lacking previous neoplasia and who also had a negative first surveillance exam.

Key Study Findings

Patients with advanced adenomas or 5 or more non advanced adenomas on their index colonoscopy had an increased risk for metachronous advanced neoplasia at the second surveillance colonoscopy. The risk was not mitigated when adjusting for endoscopists' detection rates or known risk factors such as smoking or BMI. These data support the USMSTF recommendation of a 5-year follow-up for these patients.

Caution

The low racial diversity in New Hampshire may decrease the generalizability of the findings. Thus, more data are needed in other more racially diverse populations.

My Practice

I follow the USMSTF for CRC recommendations for post polypectomy which currently suggest a 5-year follow up for these patients. These data support that recommendation by demonstrating that the risk for these patients is elevated at second surveillance colonoscopy and is independent of known risk factors as well as the adenoma detection rates of the endoscopists performing the colonoscopies.

For Future Research

These data should be validated in other populations. In addition, the risk for the third surveillance colonoscopy should be evaluated.

Conflict of Interest

Dr. Anderson had no financial conflict of interest.

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