Gallbladder Removal Associated with Lower Likelihood of Ulcerative Colitis and Crohn's Disease but Increased Likelihood of Irritable Bowel Syndrome

Team A: Matthew Gracianette, MD; Joe Deckert, PhD
Team B: Kersten Bartelt, RN; Brendan Joyce
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Key Findings:

- Patients with gallstones or gallbladder inflammation who have their gallbladder removed are nearly 20% less likely to be diagnosed with ulcerative colitis or Crohn's disease than those who do not have their gallbladder removed.
- Patients who have their gallbladder removed have a 14% increased likelihood of being diagnosed with irritable bowel syndrome than those who do not have their gallbladder removed.

Gallstones are a fairly common disorder affecting around 10-15% of the US population.[1] Gallstones, also known as cholelithiasis, can also lead to inflammation or infection of the gallbladder, known as cholecystitis.[1] Many patients do not experience symptoms from gallstones, but if they develop cholecystitis, their healthcare provider may recommend removal of the gallbladder to prevent further infection or pain.[1] While gallbladder removal is generally considered to have limited influence on a patient's life, less is known about the potential influence of the gallbladder on other digestive processes.

To understand the relationship between the gallbladder and irritable bowel syndrome (IBS), ulcerative colitis (UC), and Crohn's disease, we analyzed data from 1,146,795 patients with diagnoses of cholelithiasis or cholecystitis who retained their gallbladder and compared them to 809,206 patients who went on to have their gallbladder removed. Patients with a history of IBS, UC, or Crohn's disease before having gallstones were excluded for analysis of the condition for which they had a historical diagnosis. We adjusted for patient age, race, ethnicity, Social Vulnerability Index, rural or urban classification, BMI, and various comorbidities, including cancer, HIV, cystic fibrosis, splenectomy, or organ transplants.

In the one to three years following cholelithiasis or cholecystitis diagnosis, patients who had their gallbladder removed were 19% less likely to be diagnosed with Crohn's and 18% less likely to be diagnosed with UC compared to those who did not have their gallbladder removed. In contrast, patients who had their gallbladder removed were 14% more likely to be diagnosed with IBS.

Likelihood of Digestive Disease by Gallbladder Removal Status

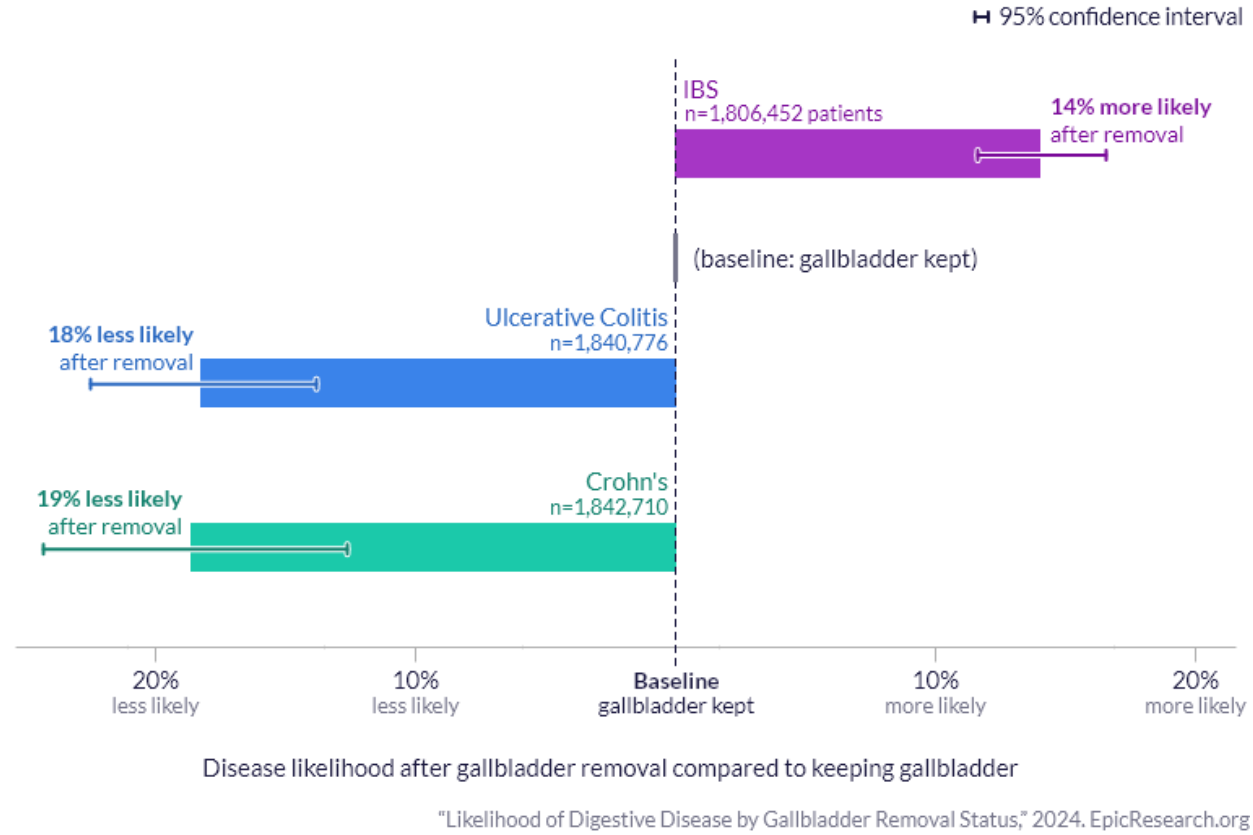

Figure 1. The likelihood of Crohn's, UC, and IBS for patients with their gallbladder removed compared to patients with their gallbladder intact.

A sensitivity analysis assessing the relationship of biliary perforation and gallbladder removal showed a high correlation, which aligns with previous findings.[2]

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 274 million patient records from 1,500 hospitals and more than 35,500 clinics from all 50 states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. National Institute of Diabetes and Digestive and Kidney Diseases. Gallstones. NIH. https://www.niddk.nih.gov/health-information/digestive-diseases/gallstones/definition-facts. Accessed August 7, 2024.
2. Gunasekaran G, Naik D, Gupta A, et al. Gallbladder perforation: a single center experience of 32 cases. *Korean J Hepatobiliary Pancreat Surg*. 2015;19(1):6-10. doi:10.14701/kjhbps.2015.19.1.6

Data Definitions

Term	Definition
Study period	1/1/2018 to 7/15/2024
Study population	Index date: A diagnosis of cholelithiasis or cholecystitis (ICD-10-CM code K80* or K81*)

	Two outpatient encounters in the three years prior to the index date and at least one face-to-face visit following the study period Index date is based on the patient's first qualifying diagnosis Patients were censored when they became **immunocompromised** or excluded if immunocompromise was documented prior to the index date. Patients were also excluded if they had a history of the outcome condition.
Cholecystectomy	A procedure with CPT code 47562-47564, 47600, 47605, 47610, or 47612 or a name containing "cholecystectomy" or "gall bladder" and "rem" but not "dev"
Outcomes	Crohn's disease: A diagnosis with ICD-10-CM code K50* IBS: A diagnosis with ICD-10-CM code K58* Ulcerative Colitis: A diagnosis with ICD-10-CM code K51* Outcome must be one to three years after the index date
Confounders	Age in years **Social Vulnerability Index** percentile **RUCA** Initial BMI value: • <30 • 30-35 • 35-40 • 40+ Comorbidities • Hypertension: ICD-10-CM code I10* • Kidney disease: ICD-10-CM code N18* • Diabetes: ICD-10-CM code E11* • Depression: ICD-10-CM code F32*, F33*, F06.31*, F06.32*, or F34.1* • Anxiety: ICD-10-CM code F40*, F41*, F93*, F94*, or F06.4* • Bipolar: ICD-10-CM code F31* • Liver disease: ICD-10-CM code G93.7, Q44.71, B1[5-19]*, E83.01, S93.4*, K57.[0-7]*, R17, or E83.11* **Race and ethnicity**
Immunocompromised	Cancer: ICD-10-CM code C* (except C44.%12*) HIV: ICD-10-CM code B20* Cystic fibrosis: ICD-10-CM code E84* Splenectomy: ICD-10-CM code Z90.81 Transplant: SNOMED code 77465005
Race and ethnicity	Patients were classified by self-reported race and ethnicity and subsequently standardized to Office of Management and Budget (OMB) race and ethnicity categorizations. Any patients with a race of Black were

	indicated as such and any patients with an ethnicity of Hispanic were indicated as such. All other patients were indicated as no for each.
Social Vulnerability Index	The social vulnerability score for the ZIP Code of the patient's most recent address
RUCA	Rural-Urban Commuting Area, a classification of geographic areas based on population density, urbanization, and daily commuting. It ranges from 1 to 10, with lower values indicating more urban areas and higher values indicating more rural areas. It was dichotomized into urban (1-6) and rural (7-10) for analysis.
Model Specifications	Cox proportional hazards

Table 1: Likelihood of Digestive Disease by Gallbladder Removal Status

	Ratio	Lower 95% CI	Upper 95% CI
Crohn's	-19%	-24%	-13%
Ulcerative Colitis	-18%	-23%	-14%
IBS	14%	12%	17%