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In this study, Swedish authors used the nationwide histopathology cohort to investigate the risk of overall and specific cardiac arrhythmias in patients with biopsy-confirmed inflammatory bowel disease (IBD). The results showed that long-term risk of developing cardiac arrhythmias was increased in patients with IBD, with the exception of bradyarrhythmias. The increased risk of developing arrhythmias in patients with IBD persisted for over 25 years after diagnosis of IBD, and was higher among patients diagnosed at 18 to 39 years.

IBD is a chronic, relapsing-remitting disease of the gastrointestinal tract, that includes ulcerative colitis, Crohn's disease, and unclassified IBD. Similar to immune-mediated inflammatory diseases, such as rheumatoid arthritis and psoriasis, IBD has been linked to increased cardiovascular disease (CVD) morbidity and mortality, including stroke, ischemic heart disease, and venous thromboembolism. Some of these studies investigated the association between IBD and arrhythmias, but, the findings were inconclusive. It is unclear whether IBD is a risk factor for overall and specific arrhythmias. A better understanding of the correlation between IBD and arrhythmias is imperative, as arrhythmias have been associated with an increased risk of cardiovascular diseases, which are the leading cause of mortality worldwide.



### ***About the study***

To explore the risk of overall and specific arrhythmias in patients with biopsy-confirmed IBD, the authors conducted a study based on the nationwide histopathology cohort Epidemiology strengthened by histopathology reports in Sweden (ESPRESSO). Patients with IBD were identified as those with at least one International Classification of Disease



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code for IBD in the Swedish National Patient Register and one biopsy record indicating IBD in the ESPRESSO during 1969 to 2017. The reference group included matched individuals and full siblings, who had to be alive, and free of IBD and cardiac arrhythmias at the time of selection.

Outcomes included overall and specific arrhythmias, such as atrial fibrillation/flutter, bradyarrhythmias, supraventricular arrhythmias, and ventricular arrhythmias/cardiac arrest. The risk of overall arrhythmia was calculated by sex, and age (<18, 18 to 39, 40 to 59, and  $\geq 60$  years), calendar period (1969 to 1989, 1990 to 1999, 2000 to 2009, and 2010 to 2019), and the number of healthcare visits (0, 1, 2 to 3, and  $\geq 4$ ).

### **The results**

The study comprised patients diagnosed with Crohn's disease ( $n = 24,954$ ), ulcerative colitis ( $n = 46,856$ ), and unclassified IBD ( $n = 12,067$ ), as well as matched reference individuals and IBD-free full siblings. Patients with IBD had a higher prevalence of other previous diseases, such as ischemic heart disease, heart failure, stroke, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD, compared with reference individuals.

During a follow-up period of approximately 10 years, cardiac arrhythmias were detected in 7.6% of patients with Crohn's disease ( $n = 1,904$ ), in 8.9% of patients with ulcerative colitis ( $n = 4,154$ ), and in 8.2% of patients with unclassified IBD ( $n = 990$  patients), compared with 6.7%, 7.5%, and 6.0% of matched reference subjects, respectively. The highest relative risk of cardiac arrhythmias was observed shortly after the diagnosis of IBD.

The incidence of arrhythmias was increased in patients with Crohn's disease (54.6 versus 46.1 per 10,000 persons), patients with ulcerative colitis (64.7 versus 53.3 per 10,000 persons), and patients with unclassified IBD (78.1 versus 53.5 per 10,000 persons), compared with reference individuals. The increased risk of developing arrhythmias in patients with IBD persisted for over 25 years after diagnosis of IBD.

Patients with IBD also had a higher risk of specific tachyarrhythmias, such as atrial fibrillation/flutter, other supraventricular arrhythmias, and ventricular arrhythmias/cardiac arrest. There was no significantly increased risk for bradyarrhythmias. The authors noted that the results of an increased risk of atrial fibrillation/flutter in patients with IBD are in accordance with previous findings.

The authors hypothesized that chronic systemic inflammatory activation appears to be the



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key component of the underlying mechanisms linking IBD to arrhythmias. Inflammatory cytokines, particularly tumor necrosis factor (TNF), interleukin(IL)-1, and IL-6, exert arrhythmogenic effects through directly affecting cardiac structural and electrical changes. They also indirectly affect the function of other systems (e.g., liver, adipose, and nervous tissue). Increased levels of C-reactive protein have been linked to atrial fibrillation development, and thromboembolic complications. As suggested in previous studies, other possible contributors, could be elevated oxidative stress, platelet and endothelial dysfunction, hypercoagulability, and alterations in the gut microbiota.

In conclusion, this study showed an increased risk of arrhythmias in patients with IBD. The authors noted that, to their knowledge, this study is the first to examine the long-term risk of newly diagnosed specific cardiac arrhythmias (except for atrial fibrillation) in patients with IBD. Healthcare professionals should be aware that patients with IBD, such as those with other extraintestinal manifestations, have a higher long-term risk of arrhythmias (in terms of absolute risk). For these patients, risk assessment of modifiable and established CVD risk factors could be considered.

### **Journal Reference**

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