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Association Between Coeliac Disease and Site-Specific Malignancy Risk: A Systematic Review and Meta-Analysis

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Abstract

Background

Coeliac disease (CD) has been associated with malignancy, although the magnitude of risk varies by cancer type. This systematic review and meta-analysis quantified site-specific cancer risk in adults with CD compared with the general population or non-CD controls.

Methods

Following PRISMA 2020 guidelines, PubMed, Embase, and Scopus were searched in April 2025. Eligible cohort and case-control studies reported ORs, RRs, HRs, or SIRs with 95% confidence intervals for cancer outcomes. We independently screened studies, extracted data, and assessed risk of bias using ROBINS-E. Effect estimates were harmonised to odds ratios using a rare-disease approximation, and random-effects meta-analyses were performed using restricted maximum likelihood with Hartung-Knapp adjustment.

Results

Of 14,694 records identified, 31 studies met the inclusion criteria, contributing 96 study-outcome

estimates across nine cancer subgroups. The strongest associations were observed for small bowel cancer (pooled OR 20.52, 95% CI 5.33–78.99) and lymphoma/lymphoproliferative malignancies (pooled OR 7.35, 95% CI 4.57–11.81). Increased risks were also found for oesophagogastric cancer (pooled OR 2.01, 95% CI 1.41–2.88) and hepatopancreatobiliary cancers (pooled OR 1.59, 95% CI 1.21–2.08). Breast cancer risk was reduced (pooled OR 0.77, 95% CI 0.63–0.94). No significant associations were observed for colorectal, prostate, lung/respiratory, or thyroid cancers. Most analyses demonstrated moderate-to-substantial heterogeneity.

Conclusion

Adults with CD have markedly increased risks of lymphoma and small bowel cancer, with more modest increases in oesophagogastric and hepatopancreatobiliary cancers, whereas breast cancer risk is reduced. Cancer risk in CD is therefore site-specific rather than uniform across malignancies.

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