

Synopsis

Celiac disease (CD) affects about 1% of the Western population. Individuals with CD suffer increased risk of a number of comorbid conditions, including certain malignancies and diabetes mellitus type 1. The pathogenesis of CD is poorly understood. The aim of this thesis was to investigate the risk of venous thromboembolism (VTE), end-stage renal disease (ESRD), and IgA nephropathy (IgAN) in individuals with CD. These studies were carried out with the objective to obtain increased knowledge regarding CD characteristics, in order to optimally design the care of individuals with CD and identify possible groups with increased risk of CD. A separate aim of this thesis was to further investigate the pathogenesis of CD, by assessing the effect of infectious disease at time of gluten introduction on the risk of future CD.

The risk of VTE was assessed in a cohort of 14,207 individuals with a discharge diagnosis of CD. When investigating renal complications (ESRD and IgAN), studies were based on a CD cohort identified through Swedish biopsy registers (about 29,000 individuals). Cox regression was used to investigate the associations between CD and outcome data in these population-based cohort studies. For the last study, we used the All Babies in Southeast Sweden (ABIS) population-based cohort study, where parents of 9,408 children prospectively completed a diary with feeding data and parent-reported infections during the child's first year of life. The pediatric departments in the area reported children diagnosed with CD.

We found a modestly increased risk of VTE in CD (Hazard ratio, HR, 1.86; 95% Confidence interval, CI, 1.54-2.24). Individuals with biopsy-verified CD suffered a three-fold increased risk of future ESRD (HR, 2.87; 95% CI 2.22-3.71). Individuals with biopsy-verified CD also suffered increased risk of future biopsy-verified IgAN (HR, 3.03; 95% CI 1.22-7.56). Although parent-reported infections were more common among children with CD ($p=0.035$), we found no increased risk of CD among children with any reported infection (HR, 1.8; 95% CI 0.9-3.6) or gastroenteritis (HR, 2.6; 95% CI 0.2-30.8) at time of gluten introduction (analyses adjusted for age at gluten introduction, age at end of breastfeeding, and age at any infection).

We conclude that CD is associated with a modestly increased risk of VTE, and that CD is a risk factor for future ESRD and IgAN. Although absolute risks are low, our findings warrant increased awareness regarding renal function in the care of individuals with CD. Future studies should evaluate the effect of adherence to a gluten-free diet to potentially identify individuals at risk.

Infection at time of gluten introduction does not seem to be a major risk factor for future CD. In a setting where adherence to infant feeding guidelines is high, duration of breastfeeding and age at gluten introduction are no major risk factors for CD. Future studies should include longer follow-up to assess long-term effects of environmental factors during the first year of life.