Publication of the Month

October 10/09: Increased Mortality in Celiac Disease

Several studies have shown an increased risk of death in celiac disease (CD). However, the introduction of serological markers for CD which can be used for mass-screening made it possible to also find individuals with less prominent symptoms; it is therefore possible that earlier studies overestimate the risk of death in CD. There are two newly published articles on mortality in celiac disease, which we would like to present here. The first study examines mortality according to small-intestinal histopathology:

Ludvigsson JF, Montgomery SC, Ekbom A, Brandt L, Granath F
Small-Intestinal Histopathology and Mortality Risk in Celiac Disease
JAMA 2009, 302:1171-1178

In this retrospective cohort study, data were collected of 46.121 individuals: (a) 29.096 CD patients, (b) 13.306 patients with small-intestinal inflammation and (c) 3.719 with biopsy-negative but seromarker-positive latent CD. The cohort included 12,000 children. Through linkage with the Swedish Total Population Register, the risk of death in the different groups was estimated and compared with the general population (sex- and age-matched). The authors found an increased hazard ratio (HR) of 1.39 for death in CD, a HR of 1.72 in inflammation, and a HR of 1.35 in latent CD. The risk increase was also seen in children. Individuals undergoing small-intestinal biopsy in childhood had increased HRs for death. Cardiovascular disease and malignancy were the main causes of death in CD.

The second study investigated for the first time the historical prevalence and long-term outcome of undiagnosed CD:

Rubio-Tapia A, Kyle RA, Kaplan EL, Johnson DR, Page W, Erdtmann F, Brantner TL, Kim WR, Phelps TK, Lahr BD, Zinsmeister AR, Melton LJ III, Murray JA
Increased Prevalence and Mortality in Undiagnosed Celiac Disease
Gastroenterology 2009, 137: 88-93

9.133 healthy young adults at Warren Air Force Base, collected between 1948 and 1954, and 12.768 age- and gender-matched subjects from two recent cohorts were tested for tissue transglutaminase antibodies. Positives were confirmed with endomysial antibodies. Only 14 (0.2%) of the Air Force cohort were positive for CD-markers. During a follow-up period of 45 years, all-cause mortality was greater in persons with undiagnosed CD than among those who were seronegative (HR = 3.9). This is a nearly 4-fold increased risk of death for undiagnosed CD.
In the more recent cohorts 68 (0.9%) individuals with similar age at sampling and 46 (0.8%) individuals with similar years of birth were positive for anti-tissue transglutaminase. The rate of undiagnosed CD was 4.5-fold and 4-fold greater in the recent cohorts, respectively, than in the Air Force cohort. The prevalence of undiagnosed CD seems to have increased dramatically in the United States during the past 50 years.

While the Swedish study finds an only moderate increase of mortality in celiac disease patients, the US-study concentrates on undiagnosed and thus untreated CD and here the risk of death is nearly 4-fold higher than in individuals without CD. This underlines the importance of early diagnosis, e.g. by mass-screening, and the compliance of the gluten-free diet. The study of Rubio-Tapia shows the tremendous increase of the prevalence of CD during the last 50 years and considers CD as a substantial public health concern.