# Are *Helicobacter pylori* highly cytotoxic genotypes and cardia gastric adenocarcinoma linked? Lessons from Iran


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**Abstract:** BACKGROUND: Although the most extensive studies revealed the role of H. pylori VacA and CagA toxins in the development of gastric adenocarcinoma, the magnitude of this association and the correlations of vacA mosaicism and cagA status with cardia gastric adenocarcinoma (CGA) still remain controversial. OBJECTIVE: We aimed to examine the linkage of H. pylori highly cytotoxic genotypes to CGA in Iranian populations as a model. METHODS: A total of 601 Iranian patients were enrolled. Biopsies were cultured, genotyped, and anatomically and histologically classified. RESULTS: The vacA c1 genotype, but not cagA status, showed a strong association with the risk of both CGA and non-cardia adenocarcinoma (NCGA), whether the controls were non-tumors, as those with either non-atrophic gastritis or peptic ulcerations, (the OR (95%CI) was 14.11 (4.91–40.52) and 9.59 (4.06–22.65), respectively) or those with NAG (the OR (95%CI) was 10.71 (3.49–32.82) and 8.11 (3.26–20.16), respectively). The vacA c1/cagA+ genotype was significantly associated with an increased risk of NCGA, whether the controls were non-tumors or those with NAG; the adjusted risk was 4.706 (1.41–15.67) and 4.85 (1.42–16.51), respectively. CONCLUSIONS: The H. pylori vacA c1 genotype, but not cagA status, might be the first important bacterial biomarker for predicting the cardia adenocarcinoma risk in male patients aged ⩾ 55 in Iran.



**Keywords:** Helicobacter pylori, vacA c, cagA, cardia gastric adenocarcinoma, diffuse-type gastric adenocarcinoma, intestinal-type gastric adenocarcinoma

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