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Relationship between *Helicobacter pylori hopQ* genotype and clinical outcome in Asian and Western populations

Tomoyuki Ohno[*], **Mitsushige Sugimoto**[*], **Aiko Nagashima**[*], **Hiroaki Ogiwara**[*], **Ratha-Korn Vilaichone**[†], **Varocha Mahachai**[‡], **David Y Graham**[*], and **Yoshio Yamaoka**[*]

[*] Department of Medicine, Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, Texas, USA [†] Gastroenterology Unit, Department of Medicine, Thammasat University Hospital, Pathumthani [‡] Gastroenterology Unit, Department of Medicine, Chulalongkorn University Hospital, Bangkok, Thailand

Abstract

Background and Aims—Outer membrane proteins of *Helicobacter pylori* mediate important pathogen–host interactions such as colonization, adhesion and the inflammatory response. *hopQ* genotypes have been suggested to be associated with increased risk of peptic ulcer. The aim of this study was to test the relation of *hopQ* genotype to *H. pylori*-related disease and histological changes in Asian and Western countries.

Methods—*hopQ* genotype, *cagA* status and *vacA* genotype of *H. pylori* isolated from patients from Asian and Western countries were determined and the results were compared with the clinical presentation and gastric histology.

Results—Most Asian strains possessed virulent genotypes (*hopQ* type I, *vacA* s1-m1 and *cagA*-positive). In Western countries, *hopQ* type I genotype was significantly linked with *vacA* s1 and m1 genotypes and *cagA*-positive status. Inflammatory cell infiltration and atrophy scores were significantly higher in patients with *hopQ* type I strains than those with type II in Western patients. However, the *hopQ* type I genotype was not associated with an increased risk for peptic ulcer or gastric cancer, and had no additive effects to *vacA* genotypes or *cagA*-positive status.

Conclusion—The expression of multiple putative virulence factors in Asian strains likely explains the relatively high incidence of clinical outcomes including gastric cancer compared with other parts of the world. Although *hopQ* genotype did not improve the predictive value above other genotyping for development of *H. pylori*-related gastroduodenal diseases, the *hopQ* genotype might be able to add a useful virulence marker for gastroduodenal diseases.

Keywords

gastric cancer; *Helicobacter pylori*; *hopQ*; virulence factor

Correspondence: Associate Professor Yoshio Yamaoka, Department of Medicine-Gastroenterology, Molecular Pathogenesis Laboratory, Michael E. Debakey Veterans Affairs Medical Center (111D), 2002 Holcombe Boulevard, Houston, TX 77030, USA. yyamaoka@bcm.tmc.edu.
Aiko Nagashima is a visiting student from Niigata University School of Medicine, Niigata, Japan.

Introduction

Although histological gastritis is universal among *Helicobacter pylori*-infected individuals, only approximately 20% develop a clinically significant outcome such as peptic ulcer, gastric cancer and primary B-cell gastric lymphoma.[1–4] Bacterial factors that predict an increased risk for a clinical outcome development have been identified (i.e. the presence of the *cag* pathogenicity island) and there is an active search for new ones.

There is considerable variation among *H. pylori* strains isolated from individuals from different geographic regions[4–7] and the host–*H. pylori* strain interactions likely differ in relation to regulation of the resulting immune and inflammatory responses of gastric mucosa. Approximately 4% of the *H. pylori* genome encodes a diverse repertoire of outer membrane proteins (OMP) that have been grouped into five major families. The *Helicobacter* outer membrane protein (Hop) family is the largest and includes adhesins such as BabA (HopS),[8] SabA (HopP),[9] OipA (HopH),[10] AlpAB (HopB and HopC)[11] and HopQ.[12] Adherence of *H. pylori* to the gastric mucosa plays important roles in the initial colonization and long-term persistence on the gastric mucosa as well as in the intensity of the resulting inflammatory response.

Sequence analysis of *hopQ* from unrelated *H. pylori* strains has revealed two genotypes with high levels of genetic diversity (75–80% nucleotide identity) which have been classified as type I and type II.[12] In the US population with peptic ulcer, most of patients with *cagA*-positive and *vacA* s1 genotype strains also expressed the *hopQ* type I genotype.[12] This study examined the diversity of *hopQ* and its correlation to gastroduodenal diseases and gastric histology among different countries and different clinical outcomes as well as with other putative virulence factors *vacA* and *cagA*.

Methods

Patients and *H. pylori* isolates

We examined strains and tissues from *H. pylori*-infected patients from Korea, Japan, Thailand, the USA and Colombia presenting with gastric cancer, gastric ulcer, duodenal ulcer or gastritis alone (Table 1). Gastritis was defined as histological gastritis with no peptic ulcers or gastric cancer. Among 557 strains examined, 358 strains had been previously examined for *vacA* s- and m-region genotypes and *cagA* status to examine the geographic distribution of *H. pylori* strains in the world.[13] Informed consent was obtained from all patients under protocols approved by the hospitals' ethics committees.

Preparation of *H. pylori* genomic DNA

Helicobacter pylori strains were grown at 37°C on brain heart infusion (BHI) (BD Diagnostic Systems, Sparks, MD, USA) plates containing 7% horse blood (Cocalico Biological, Reamstown, PA, USA). The organisms were identified as *H. pylori* by Gram staining, colony morphology, and positive oxidase, catalase and urease reactions. Genomic DNA was extracted with the QIAamp tissue kit (QIAGEN, Santa Clarita, CA, USA) or InstaGene Matrix (Bio-Rad Laboratories, Hercules, CA, USA) according to the manufacturer's instructions. The *hopQ* genotypings (type I and type II) were determined by polymerase chain reaction (PCR) methods reported by Cao *et al.*[12] Genotypings of *vacA* s- and m-regions and *cagA* status were determined by PCR as described previously.[7,14,15]

Histology

Gastric biopsy specimens were taken from the antrum (pyloric gland area) and the corpus (fundic gland area), and were stained with hematoxylin–eosin and modified Giemsa. The

biopsy specimens were fixed in 10% buffered formalin, embedded in paraffin and cut into sequential 4-μm sections. The *H. pylori* density, activity of gastritis (neutrophil infiltration) and atrophy were graded from 0 (absent/normal) to 5 (maximal) as previously described.[16] The score is presented as the mean scores of biopsy samples from the antral and corpus areas.

It is well known that atrophic gastritis has high risk of developing into gastric ulcer and gastric cancer, and antral dominant gastritis is associated with development of duodenal ulcer; therefore, the gastritis group contained a mixture of patients, some of whom would be destined to develop severe clinical outcomes. Recently, the Operative Link on Gastritis Assessment (OLGA) staging system was advocated, in which gastritis staging combined with *H. pylori* infection provided clinically relevant information on the overall status of the gastric mucosa with implications for prognosis, therapy and management.[17,18] We therefore analyzed the risk of clinical outcomes by comparing with not only all gastritis patients, but also OLGA stage I and II subjects as a control group.

Data analysis

Statistical differences in demographic characteristics, frequencies of *hopQ* genotypes, *vacA* genotypes and *cagA* status among the different geographic groups were determined by one-way ANOVA or the χ^2-test. The effects of the *hopQ* genotypes, *vacA* genotypes and *cagA* status on the risk for developing gastric cancer and peptic ulcer in patients were expressed as odds ratios (OR) with 95% confidence intervals (CI) with reference to gastritis alone or mild gastritis alone subjects adjusted by age and sex. $P < 0.05$ was accepted as statistically significant. Calculations were carried out using StatView ver. 5.0 statistical software (SAS Institute, Cary, NC, USA).

Results

We examined 557 *H. pylori* isolates (127 strains isolated in Korea, 120 in Japan, 38 in Thailand, 173 in the USA and 99 in Colombia). The demographic characteristics including proportion of sex, mean age, clinical outcomes, mean age and frequencies of different virulence factors genotypes (*hopQ*, *vacA* s- and m-region and *cagA* status) in each country are shown in Table 1. There were significant differences of sex ratio, age and clinical outcomes among different proportions ($P < 0.01$).

Prevalence of *hopQ, vacA* genotyping and *cagA* status

hopQ type I was present in 72.5% (404 strains) and *hopQ* type II was found in 15.4% (86 isolates) (Table 1). The remaining 67 cases (12.1%) were either mixed type I and II genotypes or *hopQ* not detected by PCR and they were excluded from analyses which examined the relation between *hopQ* genotype and clinical outcome. There were no significant differences in the patterns of *hopQ*, *vacA* s-region genotypes and *cagA* status among Western countries (the USA and Colombia) or among Asian countries (Korea, Japan and Thailand) and data from different Asian or Western countries were combined into Asian and Western strains. The patterns of *vacA* m-region genotypes significantly differed in Asian ($P < 0.01$) but not in Western countries (Table 1). *hopQ* type II strains were extremely rare in Asian countries (2/255; 0.7%) compared to Western countries (84/235; 35.7%) ($P < 0.01$); no *hopQ* type II strains were observed in strains from either Japan or Thailand.

Relation between *hopQ* genotype and other virulence factors

The *hopQ* type I genotype was significantly associated with *vacA* s1, m1 genotypes and *cagA*-positive status in the Western population ($P < 0.01$; ϕ value, >0.6) (Table 2). In fact, all but two (149/151: 98.7%) *hopQ* type I strains were *cagA*-positive; however, 50% (42/84)

of *hopQ* type II strains were also *cagA*-positive (Table 2). In contrast, the ϕ value of the association between *cagA* status and *vacA* s-region genotypes was extremely high (0.897) in the Western population, suggesting that the relationship between *cagA* status and *vacA* s-region genotypes was much stronger compared with that between *hopQ* type I genotype and *cagA*-positive status, *vacA* s1 and m1 genotypes. One the other hand, in Asian countries, the majority of *H. pylori* strains showed *hopQ* type I genotype accompanied with *cagA*-positive and the *vacA* s1 and m1 genotype (Table 2).

Relation between *hopQ, vacA* genotypes or *cagA* status and clinical outcomes

To evaluate the predictive value of *hopQ* genotyping in relation to clinical outcomes we performed age- and sex-adjusted univariate logistic regression analysis. In Asian countries, no significant differences were found between *hopQ* genotypes, *cagA* status and *vacA* genotypes and gastrointestinal diseases which was as expected due to the almost universal prevalence of *hopQ* type I genotype (data not shown).

In Western countries, the prevalence of type *hopQ* I genotype was 57.5% (65/113) for gastritis patients, 70.4% (38/54) for duodenal ulcer patients, 75% (21/28) for gastric ulcer patients and 67.5% (27/40) for gastric cancer patients (Table 3). The carriage of *hopQ* type I was increased in those with peptic ulcers and gastric cancer (OR adjusted for age and sex, 1.81–2.28) but the risk was not statistically sufficient ($P = 0.11–0.15$) (Table 4). In contrast, the *vacA* s1m1 genotypes and *cagA*-positive status were significantly increased in gastric cancer (adjusted OR, 5.00 [$P < 0.01$]; and 3.26 [$P = 0.04$]) and *cagA*-positive status was also significantly increased in duodenal ulcer (adjusted OR, 2.91; $P = 0.02$) (Table 4).

When compared with gastritis patients of OLGA stage I and II who had lower risk of gastroduodenal disease development, the risk of peptic ulcer and gastric cancer developments in patients with *hopQ* type I, *vacA* s1m1 and *cagA*-positive strains significantly increased (Table 4).

Combined effects of *hopQ* genotype and other virulent factors to clinical outcomes

We evaluated the additive effects by combination analysis of *hopQ* genotype and other virulence factors as a marker to predict clinical outcome (Tables 3 and 5). In the Western population, the gastric cancer was significantly associated with combination of *hopQ* type I genotype with *vacA* s1m1 genotypes compared with *hopQ* type II genotype with *vacA* s2 genotype or *vacA* s2 genotype plus *cagA*-positive groups (adjusted OR, 3.41; $P = 0.05$) (Table 5). However, there was no additive and synergic effects with relation to peptic ulcer or gastric cancer found when the analysis was done for each virulence factor genotype (*hopQ* alone, *vacA* s and m-region alone or *cagA* status alone) and for the genotype consisting of a combination of genes (Tables 4 and 5).

When compared with gastritis patients of OLGA stage I and II, the risk of peptic ulcer and gastric cancer developments in patients with combined genotype of *hopQ* type I, *vacA* s1m1 and *cagA*-positive strains significantly increased (Table 5).

Histopathological findings in relation to *hopQ* genotype

Because the gastritis group contained a mixture of patients, some of whom would be destined to develop clinical outcomes, we performed histopathological analyses in patients with gastritis alone. In Asian countries, there was no significant association between histology and *H. pylori* factors due to most strains possessing *hopQ* type I and *vacA* s1m1 genotypes and were *cagA*-positive (data not shown). In the Western population, the *hopQ* type I, *vacA* s1m1 genotypes or *cagA*-positive status was significantly associated with increased scores of gastric mucosal atrophy and inflammatory cell infiltration in both the

antrum and the corpus compared with patients with *hopQ* type II, *vacA* s2 and m2 genotypes or *cagA*-negative status, respectively (Fig. 1 and Table 6). In contrast, there was no difference in the density of *H. pylori* among *hopQ*, *vacA* genotypes or *cagA* status (data not shown). The pathological effects by combination analysis of *hopQ* genotype and other virulence factors had no additive or synergic effect for enhanced inflammation or progression of atrophy compared with analysis of one virulence factor genotype (*hopQ* alone, *vacA* s and m-region alone or *cagA* status alone) (Table 6).

Discussion

hopQ belongs to the largest OMP family in *H. pylori* (Hop family) and some of them are known as adhesins such as BabA,[8] SabA,[9] OipA[10] and AlpAB.[11] However, the details of the physiological roles of *hopQ* are still unclear. In phylogenetic analysis, two highly divergent families of *hopQ* alleles were identified, and the *hopQ* type I alleles from Western and Asian strains were similar, and that from type II allele markedly differed.[19] Analyses of synonymous and non-synonymous nucleotide substitutions suggested that there is a positive selection for HopQ amino acid diversity.[19] Moreover, *hopQ* type II genotype was identified commonly in Western *H. pylori* strains, but rarely in East Asian strains as well as *vacA* s2 genotype and *cagA*-negative strain. Cao *et al.*[12] previously reported that the carriage of type I genotype was significantly increased in subjects with peptic ulcers in the US population, suggesting that *hopQ* might play a biological role in the gastric mucosa. In this study, we demonstrated that neither peptic ulcer nor gastric cancer were significantly related to the *hopQ* type I genotype in either Western or Asian populations. However, the carriage of *hopQ* type I genotype was significantly associated with enhanced inflammatory cell infiltration in the gastric mucosa and gastric mucosal atrophy compared with that of *hopQ* type II genotype in Western populations. However, when we evaluated the effects of the *hopQ* genotype in combination analysis with virulence factor genotypes of *cagA* and *vacA*, the risk of peptic ulcer and gastric cancer development, as well as the severity of gastric inflammation or atrophy, we found no additive or synergic effects.

The *hopQ* genotypes in nearly all East Asian strains was classified as type I such that the equilibrium between *hopQ* type I and type II in East Asian strains of *H. pylori* is markedly skewed toward type I compared to Western strains. In most Asian strains, multiple genetic virulence markers, such as *cagA*, *vacA* and *oipA*, are present in a very high proportion of cases[20–24] and our results are consistent with the notion that the *hopQ* type I genotype is linked to their presence. The expression of multiple putative virulence factors (e.g. *hopQ* type I, *vacA* s1 and m1 genotypes and *cagA*-positive) in Asian strains is associated with a high proportion of the infected population with high levels of gastric mucosal inflammation of gastric mucosa, and likely explains the relatively high incidence of clinical outcomes including gastric cancer compared with other parts of the world.

Because there was no additive effect of combined *hopQ* and *vacA* genotypes and *cagA* status in terms of outcome or severity of gastritis, the biological roles and interaction of *hopQ* and other virulence factors remain unclear. The fact that *hopQ* genotype I and *cagA*-positive status and *vacA* genotype were significantly correlated, precluded detection of a specific role for *hopQ* genotype I or II. Currently, many OMP factors whose status is closely related to *cagA/vacA* status, such as *oipA* and *babA*, are well-known virulence factors and their biological roles are gradually being confirmed. Identification of possible important biological roles will probably be best identified using animal models where the effects of specific combinations of putative virulence factors can be tested directly.

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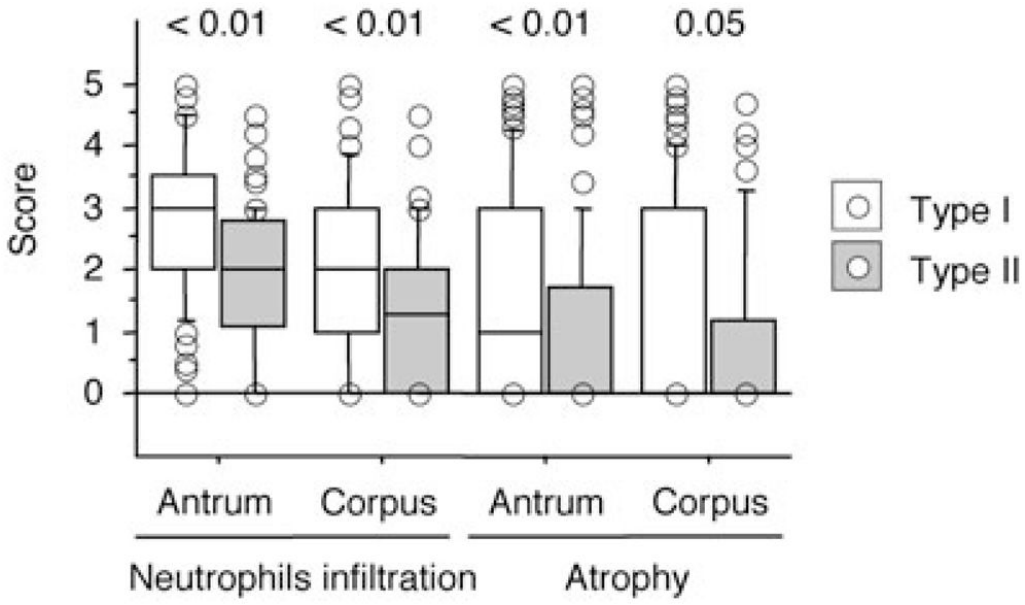

Figure 1.
The score of gastric mucosal atrophy and inflammation activity (neutrophil infiltration) in gastric antrum and corpus among different *hopQ* genotype groups in gastritis patients. *$P <$ 0.01.

Table 1

Demographic characteristics of patients and genotypes of *hopQ*, *vacA* and *cagA*

		Asian					Western		Total	*P*-value
		Korea	Japan	Thailand	Total	USA	Colombia	Total		
N		127	120	38	285	173	99	272	557	
Sex	Male/female	97/30	75/45	22/16	194/91	145/28	56/43	201/71	395/162	<0.01
Age	(mean ± SD)	47.5 ± 1.2	56.9 ± 1.3	52.1 ± 1.5	52.1 ± 0.8	49.2 ± 1.1	55.9 ± 1.5	51.0 ± 0.9	54.5 ± 0.6	<0.01
Disease	Gastritis	27.5%	22.5%	44.7%	27.7%	53.8%	33.3%	46.3%	36.8%	<0.01
	GU	21.3%	27.5%	15.8%	23.2%	17.3%	0%	11.0%	17.2%	
	DU	19.7%	23.3%	26.3%	22.1%	23.7%	26.3%	24.6%	23.3%	
	GC	31.5%	26.7%	13.2%	27.0%	5.2%	40.4%	18.0%	22.6%	
hopQ	Type I	83.5%	95.0%	86.8%	88.8%	63.0%	42.4%	55.5%	72.5%	<0.01
	Type II	1.6%	0%	0%	0.7%	27.2%	37.4%	30.9%	15.4%	
	Mix	2.4%	0%	2.6%	1.4%	7.5%	14.1%	9.9%	5.6%	
	Non-detection	12.6%	5.0%	10.6%	9.1%	2.3%	6.1%	3.7%	6.5%	
vacA	s1m1	87.4%	97.5%	20.5%	88.1%	66.6%	65.7%	63.6%	76.1%	<0.01
	s1m2	12.6%	2.5%	39.5%	11.9%	10.5%	24.2%	16.9%	14.4%	
	s2m2	0%	0%	0%	0%	22.9%	10.1%	19.5%	9.5%	
cagA	Present	97.6%	100%	100%	98.9%	85.0%	79.8%	83.1%	91.2%	<0.01
	Absent	2.4%	0%	0%	1.1%	15.0%	20.2%	16.9%	8.8%	

DU, duodenal ulcer; GC, gastric cancer; GU, gastric ulcer; mix, mix type of *hopQ* type I and type II; SD, standard deviation.

Table 2

Relationship between *hopQ* genotype and status of other virulence factors of *Helicobacter pylori*

	Virulence factor		*hopQ* type I	*hopQ* type II	*P*-value	ϕ value	Contingency value
Asian population	*cagA*	Positive	251	2	0.90	−0.008	0.008
		Negative	2	0			
	vacA s-region	s1	273	2	1.00	–	–
		s2	0	0			
	vacA m-region	m1	223	2	0.60	−0.032	0.032
		m2	30	0			
Western population	*cagA*	Positive	149	42	< 0.01	0.613	0.513
		Negative	2	42			
	vacA s-region	s1	148	37	< 0.01	0.731	0.528
		s2	3	47			
	vacA m-region	m1	129	21	< 0.01	0.609	0.489
		m2	22	63			

Table 3

Prevalence of different virulence factors in gastroduodenal diseases in Asian and Western populations

		Asian				Western			
		Gastritis (*n* = 66)	**GU (*n* = 64)**	**DU (*n* = 56)**	**GC (*n* = 69)**	**Gastritis (*n* = 113)**	**GU (*n* = 28)**	**DU (*n* = 54)**	**GC (*n* = 40)**
hopQ	Type I	66 (100%)	64 (100%)	56 (100%)	67 (97.1%)	65 (57.5%)	21 (75.0%)	38 (70.4%)	27 (67.5%)
	Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (29%)	48 (42.5%)	7 (25.0%)	16 (29.6%)	13 (32.5%)
vacA	s1m1	58 (87.9%)	57 (89.1%)	44 (78.6%)	66 (95.7%)	64 (56.6%)	18 (64.2%)	33 (61.1)	34 (85.0%)
	s1m2	8 (12.1%)	7 (10.9%)	12 (21.4%).	3 (4.3%)	20 (17.7%)	5 (17.9%)	11 (20.4%)	0 (0.0%)
	s2m2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	29 (25.7%)	5 (17.9%)	10 (18.5%)	6 (15.0%)
cagA	Present	66 (100%)	64 (100%)	54 (96.4%)	69 (98.7%)	85 (75.2%)	25 (89.3%)	47 (87.0%)	34 (85.0%)
	Absent	0 (0.0%)	0 (0.0%)	2 (3.5%)	1 (1.3%)	28 (24.8%)	3 (10.7%)	7 (13.0%)	6 (15.0%)
Combination									
hopQ + *vacA*	Type I-s1m1	58 (87.9%)	57 (89.1%)	44 (78.6%)	64 (92.8%)	57 (50.4%)	18 (64.3%)	27 (50.0%)	27 (67.5%)
	Type II-s2m2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	27 (23.9%)	5 (17.9%)	9 (16.7%)	6 (15.0%)
	Others	8 (12.1%)	7 (10.9%)	12 (21.4%)	5 (7.2%)	29 (25.7%)	5 (17.9%)	18 (33.3%)	7 (17.5%)
hopQ + *cagA*	Type 1-positive	66 (100%)	64 (100%)	54 (96.4%)	67 (97.1%)	64 (56.6%)	21 (75.0%)	37 (68.5%)	27 (67.5%)
	Type II-negative	0 (0.0%)	0 (0.0%)	2 (3.8%)	0 (0.0%)	21 (18.6%)	4 (14.3%)	10 (18.5%)	7 (17.5%)
	Others	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.9%)	28 (24.8%)	3 (10.7%)	7 (13.0%)	6 (15.0%)
hopQ + *vacA; cagA*	Type I-s1m1-positive	58 (87.9%)	57 (89.1%)	43 (76.8%)	64 (92.8%)	57 (50.4%)	18 (64.3%)	27 (50.0%)	27 (67.5%)
	Type II-s2m2-negative	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	26 (23.0%)	3 (10.7%)	6 (11.1%)	6 (15.0%)
	Others	8 (12.1%)	7 (10.9%)	13 (23.2%)	5 (7.2%)	30 (26.6%)	7 (25.0%)	19 (38.9%)	7 (17.5%)

DU, duodenal ulcer; GC, gastric cancer; GU, gastric ulcer.

Table 4

Sex- and age-adjusted risks for peptic ulcer and gastric cancer in relation to *hopQ* type I genotype in Western population

	Duodenal ulcer (*n* = 54)				Gastric ulcer (*n* = 28)				Gastric cancer (*n* = 40)			
	n	**OR**	**95%CI**	***P*-value**	***n***	**OR**	**95%CI**	***P*-value**	***n***	**OR**	**95%CI**	***P*-value**
vs gastritis patients (*n* = 132)												
hopQ type I (vs type II)	38	1.81	0.89–3.68	0.10	21	2.28	0.84–6.16	0.10	27	1.87	0.79–4.41	0.15
vacA s1m1 (vs s2m2)	40	1.90	0.82–4.41	0.13	19	1.78	0.56–5.70	0.33	42	5.00	1.62–15.45	< 0.01
cagA positive (vs. negative)	60	2.91	1.16–7.29	0.02	27	2.91	0.76–11.16	0.12	43	3.26	1.09–9.77	0.04
vs OLGA stage I and II (*n* = 92)												
hopQ type I (vs type II)	38	2.74	1.26–5.94	0.01	21	3.61	1.26–10.36	0.02	27	2.95	1.15–7.55	0.02
vacA s1m1 (vs s2m2)	40	2.99	1.17–7.67	0.02	19	2.71	0.77–9.50	0.12	42	8.38	2.37–29.60	< 0.01
cagA positive (vs. negative)	60	4.68	1.72–12.70	< 0.01	27	4.39	1.07–17.91	0.04	43	5.51	1.63–18.58	< 0.01

95%CI, 95% confidence interval; OLGA, Operative Link on Gastritis Assessment; OR, odds ratio.

Table 5

Sex- and age-adjusted risks for peptic ulcer and gastric cancer in relation to combination of *hopQ* type I genotype with *vacA* and/or *cagA* status in Western population

	Duodenal ulcer (*n* = 54)				Gastric ulcer (*n* = 28)				Gastric cancer (*n* = 40)			
	n	**OR**	**95%CI**	***P*-value**	***n***	**OR**	**95%CI**	***P*-value**	***n***	**OR**	**95%CI**	***P*-value**
vs gastritis patients (*n* = 132)												
hopQ type I + *vacA* s1m1	27	1.46	0.59–3.64	0.42	18	1.71	0.52–5.63	0.38	27	3.41	1.03–11.30	0.05
hopQ type I + *cagA* (present)	37	1.45	0.61–3.44	0.40	21	2.63	0.67–10.39	0.17	27	2.30	0.73–7.29	0.16
hopQ type I + *vacA* s1m1 + *cagA* (present)	27	2.24	0.80–6.34	0.48	18	2.98	0.73–12.18	0.13	27	3.62	1.06–12.31	0.04
vs OLGA stage I and II (*n* = 92)												
hopQ type I + *vacA* s1m1	27	2.63	0.96–7.20	0.06	18	3.27	0.91–11.76	0.07	27	6.97	1.84–26.40	< 0.01
hopQ type I + *cagA* (present)	37	2.35	0.92–6.03	0.08	21	4.50	1.07–18.94	0.04	27	4.18	1.18–14.81	0.03
hopQ type I + *vacA* s1m1 + *cagA* (present)	27	4.36	1.36–13.98	0.01	18	5.93	1.32–26.60	0.02	27	7.49	1.90–29.58	< 0.01

95%CI, 95% confidence interval; OLGA, Operative Link on Gastritis Assessment; OR, odds ratio.

Table 6

Pathological evaluation of*Helicobacter pylori* virulence factor genotype status

	Antrum		Corpus	
	High virulent factor	**Low virulent factor**	**High virulent factor**	**Low virulent factor**
Neutrophil infiltration	NA	NA	NA	NA
hopQ type I/type II	2.78 ± 0.10*	1.91 ± 0.12	2.02 ± 0.10*	1.38 ± 0.12
vacA s1m1/s2m2	2.70 ± 0.09*	1.74 ± 0.15	2.02 ± 0.09*	1.13 ± 0.16
cagA positive/negative	2.62 ± 0.08*	1.70 ± 0.16	1.89 ± 0.08*	1.17 ± 0.17
hopQ type1-*vacA* s1m1/type II-s2m2	2.79 ± 0.11*	1.73 ± 0.17	2.11 ± 0.11*	1.22 ± 0.18
hopQ type1-*vacA* m1/type II-m2	2.76 ± 0.10*	1.65 ± 0.17	2.03 ± 0.10*	1.16 ± 0.17
hopQ type1-*vacA* s1m1-*cagA* (+)/type II-s2m2-(−)	2.79 ± 0.11*	1.67 ± 0.17	2.11 ± 0.11*	1.23 ± 0.18
Atrophy	NA	NA	NA	NA
hopQ type I/type II	1.62 ± 0.13*	0.94 ± 0.16	1.26 ± 0.14*	0.79 ± 0.15
vacA s1m1/s2m2	1.73 ± 0.13*	0.80 ± 0.16	1.40 ± 0.13*	0.71 ± 0.19
cagA positive/negative	1.55 ± 0.11*	0.66 ± 0.16	1.22 ± 0.11*	0.62 ± 0.18
hopQ type1-*vacA* s1m1/type II-s2m2	1.68 ± 0.15*	0.64 ± 0.16	1.39 ± 0.15*	0.57 ± 0.17
hopQ type1-*vacA* m1/type II-m2	1.61 ± 0.14*	0.58 ± 0.15	1.25 ± 0.14*	0.57 ± 0.16
hopQ type1-*vacA* s1m1-*cagA* (+)/type II-s2m2-(−)	1.68 ± 0.15*	0.55 ± 0.16	1.39 ± 0.15*	0.55 ± 0.17

*$P < 0.05$.