Association of *Helicobacter pylori* with Coronary Artery Disease and Myocardial Infarction Assessed by Myocardial Perfusion Imaging

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**ABSTRACT:**

**Background:** The relationship between *Helicobacter pylori* infection and coronary artery disease (CAD) has as yet not been fully examined. The myocardial perfusion imaging (MPI) stress test has proven its efficacy as an integral part of diagnosing CAD.

**Objectives:** To investigate the association between CAD and *H. pylori* infection using MPI.

**Methods:** This prospective study evaluated CAD positivity among consecutive patients referred to a tertiary medical center for a stress/rest MPI. All patients were tested for serum anti-\(H. pylori\) and CagA protein immunoglobulin G antibodies. The CAD positivity group included patients with ischemia and/or myocardial infarction (MA) on a stress MPI, coronary artery bypass graft surgery (CABG), or percutaneous coronary interventions (PCI). CAD-negative subjects were defined as participants with a normal MPI, no pathological Q waves in resting ECG tracing, and no history of CAD. Both groups were compared for *H. pylori* and CagA seropositivity. Patients’ demographic data, risk factors for CAD, and childhood socioeconomic status were recorded.

**Results:** The study group consisted of 300 consecutive patients, 170 men and 130 women; 64% (110/173) CAD-positive patients and 47% (60/127) CAD-negative participants were found seropositive for *H. pylori* infection (\(P = 0.005\)). In the adjusted analysis, *H. pylori* infection was found to be associated with CAD positivity (odds ratio 1.83, 95% confidence interval 1.06–3.17, \(P = 0.031\)), and MI (fixed perfusion defects on MPI) (OR 3.36, 95%CI 1.44–7.94, \(P = 0.005\)). No association was noted with CagA positivity.

**Conclusions:** In patients undergoing a stress MPI, serum anti-\(H. pylori\) antibodies positivity was found to be associated with CAD, independent of traditional cardiovascular risk factors.

**KEY WORDS:** *Helicobacter pylori*, CagA, coronary artery disease (CAD), myocardial perfusion scan, myocardial infarction (MI)

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Chronic inflammation plays a pivotal role in the initiation, progression and complications of coronary atherosclerosis together with major risk factors for coronary artery disease [1]. A number of seroepidemiologic studies have suggested an association between coronary atherosclerosis and chronic infections [2]. *Helicobacter pylori* infection is the most common chronic bacterial infection worldwide [3]. The infection colonizes gastric mucosa and can elicit life-long inflammatory and immune responses concurrently with the release of various bacterial and host-dependent cytotoxic substances [4]. Several studies have found an association of *H. pylori* infection with the development of CAD [4–6]; others dispute this finding [7,8]. Today, this issue is still controversial. Another disagreement among researchers is whether an infection with virulent cytotoxic strains of *H. pylori* bearing the cytotoxic-associated gene A (CagA-positive strains) is associated with CAD [9,10].

A myocardial perfusion imaging stress test is widely regarded as a clinically useful non-invasive imaging modality for diagnosing patients with suspected CAD [11]. Although coronary angiography is a valuable diagnostic test for detecting coronary artery stenosis, it does not provide perfusion or contractility data when the heart is physiologically stressed. Non-invasive stress MPI can detect myocardial ischemia, as reflected by reversible perfusion defects, important components in diagnosing atherosclerotic obstructive CAD [11], and a strong predictor of adverse outcomes such as future myocardial infarctions. MI on an MPI study is diagnosed as a non-reversible fixed defect with no significant changes in activity between post-stress and rest images [12]. MPI is an established method for non-invasively assessing the functional significance of coronary stenosis and can reveal valuable information of risk stratification. Patients with stable angina and normal MPI results have a low mortality risk and, therefore, no intervention is required [13].
We conducted a prospective study of consecutive patients referred for a stress MPI to assess the association between *H. pylori* seropositivity CagA status and CAD and to evaluate the coronary distribution of fixed or reversible perfusion defects on a stress MPI.

**PATIENTS AND METHODS**

This prospective study was approved by the Rabin Medical Center Institutional Review Board. All participants were assigned a study number and data were transferred to forms to insure confidentiality. Between 1 November 2005 and 28 February 2006 all consecutive patients aged 18 years or older who presented for a stress MPI were asked to participate in the study. Indications for MPI were angina symptoms, chest pain, suspected CAD, cardiac related symptoms or risk stratifications in patients with known CAD. Those who agreed to participate gave informed consent and were subsequently included in the study. Serology for *H. pylori* status was obtained at the time of the MPI. Demographic, clinical and procedural data and risk factors for atherosclerosis were collected prospectively following a review of the clinical record. Height and weight were measured by an experienced nurse. Patients were excluded if they had been treated for an *H. pylori* infection.

Body mass index was calculated as weight in kilograms divided by the square of the height in meters. We assessed the association between *H. pylori* seropositivity status and presence of CAD. CAD positivity was defined if one or more of the following was present: reversible and/or fixed perfusion defects on a stress MPI, coronary artery bypass graft surgery, or percutaneous coronary interventions. CAD-negative subjects were defined as participants with a normal MPI, no pathological Q waves in resting electrocardiograph tracing, and no history of CAD. The association between anti-CagA seropositivity status and CAD positivity was evaluated.

In a secondary analysis, we examined the association between *H. pylori* seropositivity status and distribution of reversible or fixed perfusion defects (interpreted as MI) in CAD-positive patients.

**CONFIDENTIAL**

The following risk factors for atherosclerosis were recorded: age, gender, diabetes mellitus, hypertension, hypercholesterolemia, family history of coronary heart disease, BMI, and history of smoking. Childhood socioeconomic status parameters included father’s income classified as below average versus average or above average, and crowding index defined as the number of persons per room during childhood.

Diabetes was defined as a history of hyperglycemia requiring previous or current pharmacological therapy. Hypertension was defined as an elevation in systolic or diastolic blood pressure (>140/90 mmHg) or the need for ongoing antihypertensive medication. Hypercholesterolemia was defined as a total cholesterol level of >200 mg/dl. Family history was positive if a first-degree relative had experienced a coronary event prior to age 55 for men and 65 for women. Ever-smoked was defined as a self-report of 10 or more packs/years of cigarette use at some point in the patient’s life.

**STRESS MPI PROTOCOL**

Prior to testing, patients were asked to discontinue anti-ischemic drugs for at least 24 hours and beta-blockers for 48 hours. All tests were conducted under fasting conditions. After insertion of an intravenous line, each patient underwent stress testing by either exercising on a treadmill (the Bruce protocol) or following the dipyridamole protocol. Heart rate, blood pressure, and ECG tracings were recorded before and at each stage of exercise, when symptoms peaked or at a maximal predicted heart rate.

The Bruce protocol is used to monitor cardiac function in exercising patients. The patient is injected with thallium-201 (3–4 mCi) when exercise peaks while continuing exercising for 30–60 seconds. The dipyridamole protocol involves injecting thallium 4 minutes after termination of a dipyridamole infusion. In our study, SPECT (single-photon emission computed tomography) imaging was performed 10 minutes after the thallium injection and again 3–4 hours later, at rest.

Additional thallium reinjection imaging was performed in patients with fixed defects. SPECT acquisition was performed with a large-field digital gamma camera (SP4-HR, Elscint Ltd., Haifa, Israel) at a 180° angle, starting at the 45° right anterior oblique angle and positioning at 6° intervals for 30 seconds per image. Redistribution images were repeated 3–4 hours after stress using the same parameters. The acquisition and processing protocols have been previously described [14].

**MPI SPECT PROCESSING**

After reconstruction of the images, two-dimensional polar plot maps were generated to assess the extent of perfusion abnormality in each of the three coronary arteries. The total extent of myocardial ischemia was expressed as a percentage of global perfusion of the left ventricle.

Perfusion defects were visually and semi-quantitatively analyzed. Defects were classified as a ‘fixed defect’ (a defect present in both resting and on stress MPI images), and a ‘reversible defect’ (a defect present only on the resting MPI image). Filling defects were diagnosed as ischemia when two contiguous slices showed reversibility or when bull’s-eye mapping showed an increase in the intensity of perfusion defects of more than 10% in the redistribution phase. Perfusion defects in the anterior wall

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BMI = body mass index  
SPECT = single-photon emission computed tomography
and septal region were allocated to the left anterior descending coronary artery, defects in the lateral wall to the left circumflex coronary artery; and inferior defects to the right coronary artery. Two nuclear cardiologists, blinded to the patient’s *H. pylori* CagA status, reached a consensus on all MPI readings.

**SEROLOGY FOR ANTI-** *H. PYLORI AND CagA ANTIBODIES**

Specimens of venous blood were obtained on the same day as the stress MPI. Samples were stored at -20°C until assayed. Immunoglobulin G antibodies against *H. pylori* infection were tested by the enzyme-linked immunosorbent assay (Orion Diagnostica, Finland). A pilot study of patients who had undergone an endoscopy at our hospital was validated and showed a sensitivity of 94%, specificity of 90%, and positive and negative predictive values of 100% and 90%, respectively. IgG antibodies against CagA protein were tested using an ELISA kit (Genesis Diagnostics Ltd, UK) according to the manufacturer's instructions.

**HIGHLY SENSITIVE C-REACTIVE PROTEIN TEST**

The stored serums were tested for highly sensitive C-reactive protein test on a Roche Integra 400 analyzer, using a latex particle enhanced immunoturbidimetric kit [15]. The analytical sensitivity (lower detection limit) of the kit was 0.0085 mg/dl (reference range 0–0.5 mg/dl). Within-day precision coefficient of variation was 4.8% at a level of 0.12 mg/dl; between-day CV was 3.0% at a level of 0.4 mg/dl.

**STATISTICAL ANALYSIS**

Continuous variables were tested for normal distribution using the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean and standard deviation and non-normally distributed variables as median and interquartile range. Categorical variables were summarized as frequencies and proportions. Continuous variables were compared using the Student *t*-test or ANOVA (comparisons between groups were done using post-hoc analysis, Scheffé’s method) for normally distributed variables and the Mann-Whitney test or Kruskal-Wallis test for non-normally distributed variables. Differences in proportions among categorical data were assessed using the chi-square or Fisher exact test.

The independent association between *H. pylori* and CAD was assessed by multivariate analysis. Variables with a *P* value of < 0.3 on univariate analysis were included in the multivariate analysis. Logistic regression was used for this purpose. Odds ratios with a 95% confidence interval were reported. The association between *H. pylori* and the distribution of reversible or fixed coronary perfusion defects in CAD-positive patients was assessed by multivariate analysis. Statistical analysis was performed using the SPSS version 19. *P* value < 0.05 was considered statistically significant.

**RESULTS**

Of the 300 patients who had undergone a stress MPI, 170 (57%) were men and 130 (43%) women; mean age was 67.2 ± 11 years; 127 patients (42%) were CAD-negative and 173 (57%) were men and 130 (42%) women; mean age was 67.2 ± 11 years; 127 patients (42%) were CAD-negative and 173 (58%) were CAD-positive. Table 1 demonstrates stratification of the patient population by absence or presence of CAD. CAD-positive patients were older and included more men than the CAD-negative subjects (*P* = 0.021, *P* < 0.001, accordingly). CagA seropositivity was not statistically different between CAD-FD patients (124/271, 46.1%) and CAD-NFD patients (43/129, 33.3%); *P* = 0.038, accordingly).

<table>
<thead>
<tr>
<th></th>
<th>CAD-negative (n=127)</th>
<th>CAD-positive (n=173)</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Helicobacter pylori</strong></td>
<td>60 (47.2%)</td>
<td>110 (63.5%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Male</td>
<td>46 (36.2%)</td>
<td>124 (71.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>34 (26.7%)</td>
<td>58 (33.5%)</td>
<td>0.210</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70 (55.1%)</td>
<td>114 (65.8%)</td>
<td>0.058</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>67 (52.7%)</td>
<td>141 (81.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history</td>
<td>28 (22.9%)</td>
<td>57 (32.9%)</td>
<td>0.038</td>
</tr>
<tr>
<td>Smoker</td>
<td>11 (8.6%)</td>
<td>16 (9.2%)</td>
<td>0.861</td>
</tr>
<tr>
<td>Age (yr), mean (SD)</td>
<td>65.4 (11.9)</td>
<td>68.5 (10.1)</td>
<td>0.021</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27.3 (5.0)</td>
<td>27.1 (3.9)</td>
<td>0.604</td>
</tr>
<tr>
<td>HsCRP, median (IRQ)</td>
<td>0.3 (0.1–0.6)</td>
<td>0.3 (0.2–0.6)</td>
<td>0.941</td>
</tr>
<tr>
<td>Crowding index, median (Q3)</td>
<td>2.0 (1.3–3.3)</td>
<td>2.0 (1.3–3.0)</td>
<td>0.882</td>
</tr>
</tbody>
</table>

**Table 1. Comparison of *H. pylori* seropositivity and risk factors for CAD between CAD-negative group and CAD positive groups**

**Note:**
- HsCRP = highly sensitive C-reactive protein
- IRQ = interquartile range
- BMI = body mass index

*H. pylori* infection was significantly higher in CAD-positive patients than in CAD-negative subjects (odds ratio 1.95, 95% confidence interval 1.2–23.11, *P* = 0.005). Diabetes mellitus, hypertension, smoking history, crowding index, HsCRP level and BMI showed no significant difference between CAD-positive and negative participants. In crude analyses, CagA seropositivity in the CAD-positive group was not statistically different from the CAD-negative group (40% vs. 48.3%, *P* = 0.294); patients with fixed defects were associated with positive *H. pylori* status (OR 2.93, 95%CI 1.50–5.75, *P* = 0.002), and CAD-positive patients with no fixed defects tended to be associated with positive *H. pylori* status (OR 1.62, 95%CI 0.97–2.69, *P* = 0.065). CagA seropositivity was not statistically different between CAD-FD (38.2%), CAD-NFD patients (42.9%) and...
Table 2. Comparison of *H. pylori* seropositivity and risk factors for CAD between CAD-negative subjects and CAD-positive patients with no fixed defects and patients with fixed defects

<table>
<thead>
<tr>
<th></th>
<th>CAD-negative (n=127)</th>
<th>CAD-positive without MI (CAD-NFD) (n=115)</th>
<th>CAD-positive with MI (CAD-FD) (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helicobacter pylori</td>
<td>60 (47.2%)</td>
<td>68 (59.1%)</td>
<td>42 (72.4%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Male</td>
<td>46 (36.2%)</td>
<td>78 (67.8%)</td>
<td>46 (79.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>34 (26.7%)</td>
<td>35 (30.4%)</td>
<td>23 (39.6%)</td>
<td>0.211</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70 (55.1%)</td>
<td>80 (69.5%)</td>
<td>34 (58.6%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>67 (52.7%)</td>
<td>87 (75.6%)</td>
<td>54 (93.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history</td>
<td>28 (22.0%)</td>
<td>38 (33.0%)</td>
<td>19 (32.7%)</td>
<td>0.117</td>
</tr>
<tr>
<td>Smoker</td>
<td>11 (8.6%)</td>
<td>8 (6.9%)</td>
<td>8 (13.7%)</td>
<td>0.328</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease, CAD-NFD = CAD-positive patients with no fixed defects, CAD-FD = CAD-positive patients with fixed defects. HsCRP = highly sensitive C-reactive protein, IQR = interquartile range

CAD-negative subjects (48.3%, P = 0.515). The prevalence of men and hypercholesterolemia was significantly higher in CAD-FD and CAD-NFD patients than in controls (P < 0.001, P < 0.001, respectively) [Table 2].

In the multivariate analysis, controlled for gender, age, diabetes, hypertension, hypercholesterolemia, and family history of CAD [Table 3], *H. pylori* seropositivity was independently associated with fixed defects versus non-CAD [Table 3]. The odds ratio for fixed defects (MI) was higher (3.36, 95%CI 1.44–7.84) than for CAD-positive patients without fixed defects (1.55, 95%CI 0.86–2.77), and CAD-positivity (1.83, 95%CI 1.06–20.2) versus CAD-negative subjects. Both men and hypercholesterolemia were independently associated with CAD-positivity, CAD without fixed defects and CAD with fixed defects [Table 3].

Table 3. Odds ratio and 95% confidence interval for coronary artery disease and CAD with and with no fixed defects from a multivariable logistic regression

<table>
<thead>
<tr>
<th></th>
<th>CAD-positive*</th>
<th>CAD-NFD*</th>
<th>CAD-FD*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>(95%CI)</td>
<td>P</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em></td>
<td>1.83</td>
<td>(1.06–3.17)</td>
<td>0.031</td>
</tr>
<tr>
<td>Male</td>
<td>6.84</td>
<td>(3.79–12.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>1.06</td>
<td>(1.03–1.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.17</td>
<td>(0.65–2.11)</td>
<td>0.607</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.22</td>
<td>(0.69–2.14)</td>
<td>0.501</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3.36</td>
<td>(1.83–6.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history</td>
<td>1.90</td>
<td>(1.00–3.61)</td>
<td>0.051</td>
</tr>
</tbody>
</table>

*vs. normal perfusion scan

Table 4. Multivariate analysis of risk factors for fixed perfusion defects (MI) in the right coronary artery territory

<table>
<thead>
<tr>
<th></th>
<th>Fixed defects in the territory of RCA vs. fixed defects in territories of other coronary arteries (n=58)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>(95%CI)</td>
</tr>
<tr>
<td><em>H. pylori</em></td>
<td>21.64</td>
<td>(2.08–224.86)</td>
</tr>
<tr>
<td>Male</td>
<td>3.68</td>
<td>(0.57–61.6)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>0.99</td>
<td>(0.93–3.06)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.34</td>
<td>(0.56–9.83)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.79</td>
<td>(0.44–7.36)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.25</td>
<td>(0.01–5.39)</td>
</tr>
<tr>
<td>Family history</td>
<td>1.74</td>
<td>(0.37–8.13)</td>
</tr>
</tbody>
</table>

RCA = right coronary artery

Fixed defects in the distribution of RCA (19/20) vs. fixed defects in the distribution of other coronary arteries in 58 patients (with MI) were significantly associated with positive *H. pylori* status on both crude (OR 12.39, 95%CI 1.50–102.56, P = 0.020) and multivariate analysis (OR 21.64, 95%CI 2.069–224.86, P = 0.010). Fixed defects in the distribution of other coronary arteries were not associated with positive *H. pylori* status [Table 4]. The presence of reversible defects (ischemia) in the distribution of coronary arteries on stress MPI was not associated with positive *H. pylori* status on crude analysis.

**DISCUSSION**

Our findings revealed a significantly higher rate of *H. pylori* seropositivity in CAD-positive patients compared to the CAD-negative patients. To the best of our knowledge, this is the first study designed to assess the association between *H. pylori* infection and CAD in a prospective study of patients who had undergone a stress MPI. MPI is an established method for non-
Invasively assessing the functional significance of coronary stenosis by minimizing any misclassification of CAD patients. The test determines the presence or absence of effort-induced ischemia (reversible defects) or MI (fixed defects), or both, in the two groups, thus providing additional and important diagnostic criteria for detecting patients with silent undiagnosed CAD. Detection of ischemia and/or MI on a stress MPI indicated the presence of CAD even in the absence of other findings.

Aiming to minimize misclassification of the presence or absence of CAD, we selected a CAD-negative group without known CAD or any ischemic findings or MI on a stress MPI. In order to adjust for confounders, we included major and well-established risk factors.

Our results indicated that H. pylori seropositivity is independently associated with CAD (OR 1.83, 95% CI 1.06–3.17) and MI (OR 3.36, 95% CI 1.44–7.84). No significant difference was found in anti-CagA seropositivity among the CAD-positive and CAD-negative groups. Our findings support a recent study by Jafarzadeh et al. [16] who reported significantly higher anti-H. pylori antibodies in the serum of 120 patients with ischemic heart disease compared to patients without ischemic heart disease. The seroprevalence and mean titer of anti-CagA IgG did not significantly differ between patient and control groups. A similar observation was reported by Pellicano and co-authors [17] who studied 223 consecutive patients with confirmed acute MI and compared them with matched controls. Anti-CagA antibodies were detected in 33.8% of infected patients with acute MI versus 26.8% in the control subjects (P = 0.17, OR 1.40, 95% CI 0.84–2.33), indicating no relationship between H. pylori infection with CagA-positive strains and ischemic heart disease.

In the present study, the association of H. pylori infection with MI was strongest with MI defined on the basis of fixed perfusion defects on MPI. The odds ratio for MI seropositivity was 2.93 (95% CI 1.50–5.75) and was largely unchanged after adjustment (OR 3.36, 95% CI 1.44–7.84), suggesting that exact adjustment for the truly relevant factors would have little effect. In addition, all CAD-negative subjects in this study had normal perfusion on the stress MPI without evidence of MI or ischemia.

Some studies included only patients with MI [5]. The results might partly reflect the relationship between H. pylori infection and CAD if the patients who presented with angina, but without MI, were not included. In the current study, however, we separately analyzed CAD-positive patients without MI and patients with MI and found that the association of H. pylori infection with MI was statistically significant while the association in CAD-positive patients without MI tended to be significant.

Infection was proposed as a cause of atherosclerosis at the beginning of this century [18]. The modern “response-to-injury” model of atherosclerosis suggests that infection could contribute to the formation of atherosclerosis via damage to vessel endothelium [19]. In addition, it has been suggested that autoimmune reactions against endogenous heat shock protein 60, an endothelial antigen, could trigger atherogenesis [20]. H. pylori contains HSP60-like subunits, and the possibility of an association between H. pylori infection and an immune response to HSP60 is under investigation.

We examined whether a relationship exists between prevalence of H. pylori infection and specific territories of coronary vessels. We examined whether a relationship exists between prevalence of H. pylori infection and specific territories of coronary vessels. A significant link was found on the MPI between H. pylori seropositivity in patients with fixed defects in the distribution of the RCA. This association remained statistically significant after adjustment for CAD risk factors (OR 21.64, 95% CI 2.08–224.86, P = 0.010). Perfusion defects in the distribution of the other coronary arteries showed no correlation with H. pylori infection (data not shown). Confidence intervals were wide-ranging, leaving room for the possibility that H. pylori could have a moderate effect on MI risk in RCA territory, as this territory is adjacent to the stomach and hypothetically might be associated with the gastric colonization of H. pylori. Thus, additional prospective studies with a larger number of patients should be performed to possibly narrow the confidence intervals found in this study.

Many previous studies did not adjust for socioeconomic status, known to affect the risk of CAD and H. pylori carrier status. How childhood socioeconomic deprivation can increase the risk of CAD is not fully known. Acquisition of H. pylori infection in childhood could be one of the reasons. We included data on three individual markers of childhood low socioeconomic status (father’s low income, father’s occupation as a manual laborer, and high household density during childhood) for both groups and found no correlation between H. pylori seropositivity, crowding at childhood, and CAD. We believe that the relationship between H. pylori infection and the risk of CAD cannot be entirely explained by low socioeconomic status, although a limitation of our study is the lack of more detailed information relating to childhood socioeconomic status.

In addition, it is well known that infections are able to modify serum lipids. Alterations of the lipid metabolism due to chronic H. pylori infections could represent an atherogenic link. Hyperlipidemia, especially hypercholesterolemia, is an established risk factor of atherosclerosis. In this study, hypercholesterolemia was independently associated with CAD.

**Limitations**

A possible limitation of our study is that it was performed on a selected population referred for a stress MPI in order to diagnose ischemia in a suspected unknown CAD patient as well as patients with known CAD, thus our results may not necessarily apply to the general population.

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HSP60 = heat shock protein 60
CONCLUSIONS
This prospective study among consecutive patients who had undergone a stress MPI supports the hypothesis that chronic infections may contribute to an accelerated atherosclerotic process in the coronary arteries, suggesting an independent association of seropositivity for H. pylori and risk of subsequent CAD and MI.

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References

Modeling the mitochondrial cardiomyopathy of Barth syndrome with induced pluripotent stem cell and heart-on-chip technologies

Study of monogenic mitochondrial cardiomyopathies may yield insights into mitochondrial roles in cardiac development and disease. Wang and collaborators combined patient-derived and genetically engineered induced pluripotent stem cells (iPSCs) with tissue engineering to elucidate the pathophysiology underlying the cardiomyopathy of Barth syndrome (BTHS). BTHS, a mitochondrial disorder caused by mutation of the gene encoding tafazzin (TAZ), Using BTHS iPSC-derived cardiomyocytes (iPSC-CMs), the authors defined metabolic, structural and functional abnormalities associated with TAZ mutation. BTHS iPSC-CMs assembled sparse and irregular sarcomeres, and engineered BTHS 'heart-on-chip' tissues contracted weakly. Gene replacement and genome editing demonstrated that TAZ mutation is necessary and sufficient for these phenotypes. Sarcomere assembly and myocardial contraction abnormalities occurred in the context of normal whole-cell ATP levels. Excess levels of reactive oxygen species mechanistically linked TAZ mutation to impaired cardiomyocyte function. This study provides new insights into the pathogenesis of Barth syndrome, suggests new treatment strategies, and advances iPSC-based in vitro modeling of cardiomyopathy. Nature Med 2014; 20: 616

Eitan Israeli