Helicobacter Pylori Infection and Acute Myocardial Infarction

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ABSTRACT

The aim of this investigation was to determine whether H. pylori *infection is an independent risk factor for acute myocardial infarction (AMI), determine is there a link between* H. pylori *infection and severity of disease. In this prospective, single centre study, were enrolled 100 patients with AMI and control group was consisted 93 healthy individuals. The results of this study showed no difference between* H. pylori *seropositivity distribution in the investigate and control group (29 vs. 26 %) and there was no significant difference on the severity of the disease. There was significant association in the patients with three and more risk factors, where the patients with lower blood pressure (124.4/77.4 vs. 145.9/87.7 mmHg) and better controled diabetes (HbA1c 6.1 % vs. 6.9 %) had greater risk for AMI if they are* H. pylori *seropositive. The large multicentric trials would be needed to define a precise role of* H. pylori *infection on the developement of AMI.*

Key words*: Helicobacter pylori infection, acute myocardial infarction*

Introduction

There are several studies which showed that chronic infections may be associated with onset of atherosclerosis and subsequently coronary artery disease[1,2]. H. pylory infection may couse chronic low grade infection which lead to production of different vasoactive substances with direct influence on coagulation system and may couse prothrombotic status with developement of coronary heart disease (CHD) and onset of acute myocardial infarction (AMI)[3,4]. *H. pylori* infection cuold induce changes in cogulation with elevated serum levels of fibrinogen, prothrombin fragments, plasminogen-activating inhibitor-1 (PAI-1), and factor VII. Several other machanisms may be responsible for onset of CHD and AMI like elevated concentrations of tumor necrosis factor- , (TNF-), interleukin-6, (IL-6) and interleukin-8 (IL-8), lipid profile changes[5–8]. *H. pylori* DNA was isolated by polimerase chain reaction from atherosclerotic plaque and it is reasonable to purpose direct effect on lession pregression and activation of inflammation can lead to acute coronary syndromes[9,10]. Still, there are controversis about role of *H. pylori* infection in CHD and AMI, with many studies pro[11–16] and many contra that association[17–21]. *H. pylori* infection is associated with some socioeconomic factors, particulary low social grade which can contribute to higher incidence of cardiovascular diseases. The purpose of this study was to determine whether *H. pylori* infection is an indipendent risk factor for AMI, determine is there a lin between *H. pylori* infection and severity of disease, find out is there link between *H. pylori* infection and well known risk factors for CHD and AMI.

Material and Methods

In this prospective study were enrolled 100 patients admitted in single centre with AMI. All subjects had given informed consent to inclusion in the study and research was carried out according with principles of Declaration of Helsinki. Control group was consisted of 93 healthy participants. Exclusion criteria were well known ulcer disease, treatment for ulcer disease in the last 12

months and eradication therapy for *H. pylori* in the last 12 months.

Diagnosis for AMI was established in patients with chest pain in the last 24 hours followed by ECG changes and elevated heart enzymes: creatine kinaze (CK), its isoenzyme MB (CK-MB) and troponin I. A 97 of total 100 patients with AMI undergoing cardiac catheterization and percutane coronary intervention (PCI), coronary angiograms were read by an expirienced invasive cardiologists who were blinded to the patients *H. pylori* status. Angiograms were graded as normal if there was no affected coronary artery or abnormal. Abnormal angiograms were further subdivaded into groups according to the number of affected vessels in the: single, double or triple vessel disease.

Analyzed risk factors for CHD included hypertension, diabetes, hyperlipidemia, obesity, gender and cigarette smoking. Hypertension was considered in the patients with arterial pressure >140/90 mmHg, or were being treated with antihypertensive drugs or dietary modifications. Diabetic patients were considered to have diabetes if they have had fasting glucose >6.4 mmol/L, HbA1c> 6.0% or were taking insulin, hypoglicemic agents or dietary modification to control the disease. Hyperlipidemia were considered in patients with serum cholesterol levels >5.2 mmol/L or receiving lipid lowering agents. Obesity status was defined followed by body mass index (BMI): subjects with BMI <24 were considered normal, BMI 25–29 were considered overweight and BMI >30 were considered obese. Smoking as risk facor were no considered in patients who had stopped smoking >20 years ago or who were <30 years of age when they stopped smoking.

All subjects (patients with AMI and control group) underwent an enzyme-linked Immulite (chemilumines-cent) analyzer IgG serologic test for *H. pylori* diagnosis (Diagnostic Products Corp., Los Angeles, CA, USA). The test has a sensitivity of 97% and a specificity of 98%.

Control group consists of healthy subjects and they were excluded if they had history of peptic ulcer disease, received therapy for eradication *H. pylori* or received acid-suppresive drugs in last 12 months.

Statistical analysis is carried out by using SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc., Chicago, IL, USA). For comparing differencies between sets of results we used t–tests and for associations between variables correlation methods. Regression analysis was used for prediction of *H. pylori* seropositivity, ^{2}-test was used to find out differences between frequency of risk factors. Results are shown by average values with standard deviations. A value of p<0.05 was considered statistically significant.

Results

Investigate group was consisted of 100 individuals admitted in coronay care unit for AMI with ST segment elevation (STEMI) or without ST segment elevation (non-STEMI). Demographic characteristics of patients are listed in the Table 1.

There were 67 men (67%) and 33 women (33%) with average age of 64.7 years. There were 77 % hypertensive patients with average values of 144/88 mmHg, 59% patients were diabetic and average values od serum glucose in whole group were 8.6 mmol/L with HbA1c levels of 6.4%. Th whole group were overweight with average BMI values 27.3 kg/m², there were 67% of patients with hyperlipidemia and average cholesterol levels in whole group were 5.8 mmol/L. Smoking as a risk factor was

TABLE 1
DEMOGRAPHIC CHARACTERISTICS OF PATIENTS

	Number	$\overline{X}$	Min	Max	SD
Age	100	64.74	35.00	87.00	11.34
Gender	100	1.33	1.00	2.00	0.47
Hypertension (grade)	100	1.02	0.00	2.00	0.70
Systolic pressure (mmHg)	100	143.75	80.00	250.00	33.49
Diastolic pressure (mmHg)	100	87.95	50.00	140.00	18.18
Dyslipidemia (yes/no)	100	0.67	0.00	1.00	0.47
Cholesterol (mmol/L)	100	5.77	0.71	8.60	1.30
Glucose (mmol/L)	100	8.59	5.00	22.70	3.79
Diabetes (yes/no)	100	0.41	0.00	1.00	0.49
HbA1c (%)	100	6.37	5.20	11.80	1.32
Body mass index (kg/m²)	100	27.29	20.00	42.00	3.78
Smoking (yes/no)	100	1.50	1.00	2.00	0.50
STEMI/nonSTEMI	100	1.44	1.00	2.00	0.50
Coronary angiography (number of affected vessels)	97	1.82	0.00	3.00	0.94
Troponin I (ng/mL)	100	33.76	0.60	234.20	46.72
H. pylori	100	1.71	1.00	2.00	0.46

TABLE 2
COMPARISON OF PATIENTS WITH *H. PYLORI* AND 3 RISK FACTORS (RF) WITH THOSE WITHOUT *H. PYLORI* BUT WITH 3 RF FOR CORONARY ARTERY DISEASE

	3 RF + HP	3 RF – HP	t-value	df	p	SD – 1	SD – 2
Syst	124.4000	145.8571	–2.55639	58	0.013217	31.86299	32.18708
Diast	77.4000	87.7143	–2.36242	58	0.021532	17.91880	15.73414
Cholest	5.9160	6.1000	–0.59127	58	0.556640	0.76631	1.41234
Glucose	7.7040	10.4429	–2.45872	58	0.016949	2.46416	5.15588
HbA1c	6.0800	6.9343	–2.35590	58	0.021879	0.77028	1.68888
BMI	28.5200	27.6857	0.91203	58	0.365530	3.28024	3.63619
Cor.ang.	1.6000	1.8788	–1.14147	56	0.258532	1.08012	0.78093
Trop.	27.1520	29.6457	–0.24420	58	0.807934	34.46445	41.90085

present in the 50% of patients. A total of 56 patients (56%) had STEMI *vs.* 44 (44%) with nonSTEMI. In 97 pateints with coronary angiography there were 1.8 average affected coronary arteries. Average troponin levels were 33.8. Procalcitonin as a marker for infection was in normal levels in both patients and control group, independent of *H. pylori* seropositivity. There were 29% patients seropositive for *H. pylori* versus 26% in control grouup of healthy individuals and there was no significant statistical difference in *H. pylori* infection between two groups, also there was no significant differencies between men and women (30 *vs.* 27%). When we compare men and women we find out that women were 5.5 years younger than men (62.9 *vs.* 68.4 year) and there were significant lower number of women (p=0.001) who had smoking as a risk factor (27% *vs.* 61%). There were no significant diferrences between men and women in distribution of hypertension, diabetes, obesity, hyperlipidemia, STEMI and number of affected coronary vessels.

When we want to find out possible relationship of *H. pylori* infection to severity of coronary artery disease, we found 29% patients with triple vessel disease, 32% with double vessel disease, 32% with single vessel disease and 7% without significant stenosis of coronary arteries. There was not significant difference in seroprevalence of *H. pylori* infection between patients with no coronary artery disease, single or triple vessel disease. Only signifi-

cant difference according to the ^{2}-test was noticed in group of double vessel dissease where there was small number of seropositive *H. pylori* patients (only 3 patients), so that isolated result of double vessel disease is statisticaly nonconfidential. The results are shown on Figure 1.

Comparing the results of patients with three and more risk factors according to the *H. pylori* seropositivity we got significant difference in systolic and diastolic blood pressure (p=0.01, p=0.02), and diabetes (serum glucose p=0.01, HbA1c p=0.02). The results are shown in Table 2.

Discussion

Several studies suggested that *H. pylori* couse low grade chronic bacterial infection which lead to production of different vasoactive substancies linked to the developement of coronary heart disease. *H. pylori* infection may increase risk for acute myocardial infarction through the changes in the lipid status with lower HDL cholesterol values and elevated serum trigliceride values, changes in the coagulation parameters with elevated fibrinogen, prothrombin fragments, plasminogen-activating inhibitor 1 (PAI-1) and factor VII, increased concentrations of markers of inflammation as a tumor necrosis factor – (TNF-), interleukin-6 (IL-6), interleukin-8 (IL-8) and others. Also it has been noticed possible direct effect on the stability of the atherosclerotic plaque. Both *H. pylori* infection and coronary artery disease are associatted with lower socioeconomic status and their frequency is higher with older age[8].

Some studies find association of *H. pylori* infection and acute coronary syndromes. In those studies there were reletively high persent of *H. pylori* seropositivity in both, patients and controls. Miyazaki et al. in 2006 reported 87.9% *H. pylori* seropositive patients *vs.* 66.7% in control group in Japanese population. In Italian study from 2003 Pelicano et al. find 81% seropozitive patients with acute coronary syndrome *vs.* 53% in control group. These results were confirmed by another Italian study performed by Lenzi et al. who find 78.7% *H. pylori* seropositive patients *vs.* 76% in control group. Whincup et al.
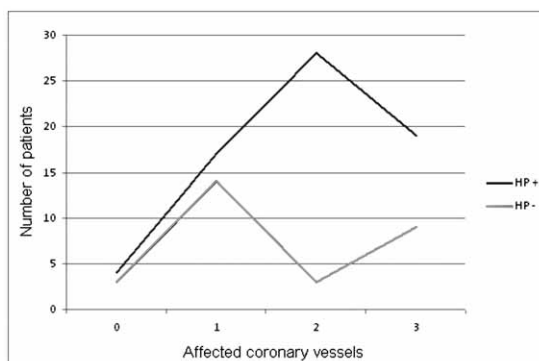

Fig. 1. Number of affected coronary vessels according to the H. pylori seropositivity.

in British study from 1996 found 70% seropositive patients with coronary hearth disease *vs*. 57% in controls[11,12,22,23].

Despite these results in the studies which did not show association of *H. pylori* infection and coronary artery disease there was lower incidence of *H. pylori* seropositivity in patients and controls. Kurshid et al. found 45% seropositive in patients and 47% in controls, Folsom et al. found 51% *H. pylori* seropositivity in both groups. Tsai et al. in Taiwanian study found 69% seropositivity in investigate *vs*. 72% in controls[4,17,19]. In resent Croatian study performed by Včev et al. showed higher seroprevalence of *H. pylori* infection in patients with coronary artery disease compared to controls (78.8 *vs*. 58.3%), but *H. pylori* infection was not associated with coronary artery disease risk factors (smoking, obesity, diabetes, hypertension, cholesterol and socioeconomic status)[20].

In our study we found 29% *H. pylori* seropositive patients with acute myocardial infarction *vs*. 26% seropositive healthy controls. There was not significant statistical difference (p=0.08) between these groups which suggest that *H. pylori* infection is not independent risk factor for acute myocardial infarction. In our study there was significantly lower incidence of *H. pylory* infection in both patients and controls, particulary due to exclusion criteria of all participants with known gastric disease, or receiving therapy for gastric disease or eradication for *H. pylori*, particulary for better socioeconomic conditions compare to postwar period in Croatia in recent studies[23]. When we compare these seropositivity results with *H. pylori* positivity of 36% according to the Pronto Dry test in all patients underwent gastroscopy in one year in same center, there is still low incidence of *H. pylory* infection in this mediterranean part of Croatia.

Investigating relationship of *H. pylori* infaction and severity of coronary artery disease according to the number of affected vessels (none, single, double and triple vessel dissease) we did not found strong association. Only weak statistical significance was found in subgroup of double vessel disease, where *H. pylori* infection was in favor for patients, but with only three *H. pylori* seropositive patients. Similar results reports Kurshid et al. in prospective study with patients underwent coronary angiography. Also Tsai et al. did not find assotiation of *H. pylori* infection and severity of coronary artery disease, even there was higher incidence of triple vessel disseease in *H. pylori* seropositive patients[4,19].

In the patients with 3 and more risk factors for AMI (hypertension, diabetes, hyperlipidemia, obesity and smoking) we found *H. pylori* infection as an independent risk factor. Patients with lower blood pressure and better controlled diabetes have higher risk for myocardial infarction if they are *H. pylori* seropositive. There was significant statistical difference (p<0.05) for systolic and diastolic blood pressure (124/77 *vs*. 146/88 mmHg) and diabetes (serum glucose 7.7 *vs*. 10.4 mmol/L and HbA1c 6.1 *vs*. 6.9%) in patients with 3 and more risk factors who were *H. pylori* seropositive *vs*. patients who were not seropositive.

In summary, we can conclude that *H. pylori* infection is a primarily localized infection with weak systemic implications. The present results indicate that *H. pylori* infection is not an independent risk factor for acute myocardial infarction and it is not risk factor for severity of dissease. But in the patients with three and more well known risk factors *H. pylori* infection could have impact as an independent risk factor for AMI. Further studies are needed to define a precise role of *H. pylori* infection on the developement of acute myocardial infarction and coronary artery disease.

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INFEKCIJA HELICOBACTER PYLORI I AKUTNI INFARKT MIOKARDA

S A Ž E T A K

Cilj ovog istraživanja je bio odrediti da li infekcija *Helicobacter pylori* predstavlja neovisan faktor rizika za akutni infarkt miokarda, odrediti da li postoji povezanost težine infarkta s infekcijom *H. pylori*. U ovu prospektivnu studiju provedenu u jednom centru uključeno je 100 bolesnika s akutnim infarktom miokarda i 93 zdrava ispitanika u kontrolnoj skupini. Rezulati studije nisu pokazali značajnu razliku u distribuciji infekcije *H. pylori* u ispitanika i kontrolnoj skupini (29 *vs.* 26%) i nije nađena značajna razlika u težini bolesti prema seropozitivnosti na *H. pylori*. Značajna razlika nađena je kod bolesnika s tri i više faktora rizika pri čemu su bolesnici s nižim krvnim tlakom (124,4/77,4 *vs.* 145,9/87,7 mmHg) i bolje reguliranim dijabetesom (HbA1c 6,1 *vs.* 6,9%) imali veći rizik za infarkt miokarda ako su *H. pylori* seropozitivni. Potrebne su veće multicentrične studije za određivanje precizne uloge *H. pylori* infekcije u nastanku infarkta miokarda.