

## Short Communication

## Detection of *Chlamydomphila pneumoniae* IgG in blood samples taken from coronary sinus during bypass surgery

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Chronic infection may promote arterial inflammation, thereby contributing to the initiation or progression of atherosclerosis. *Chlamydomphila pneumoniae* is an obligate intracellular human respiratory pathogen. It has been suggested that coronary atherosclerosis may be an autoimmune process triggered by an infectious agent, most likely *C. pneumoniae*. The purpose of the present study was to investigate the effects of coronary artery bypass surgery on *C. pneumoniae* IgG detection in blood samples taken from coronary sinus. Forty-two patients (aged 39 to 83 years) who were consecutive candidates of elective coronary artery bypass surgery for *de novo* lesions (coronary angiography showing  $\geq 70\%$  lumen diameter stenosis in at least one epicardial coronary artery) were enrolled in this study. Blood samples were drawn from an antecubital vein immediately before the operation and from the coronary sinus during coronary artery bypass surgery for determination of specific IgG antibodies against *C. pneumoniae*. *C. pneumoniae* IgG was negative in all blood samples obtained immediately before coronary artery bypass surgery. In terms of blood samples drawn from the coronary sinus during coronary artery bypass surgery, there were no statistically significant differences between *C. pneumoniae* IgG negative and positive groups with respect to age, gender, hypertension, diabetes mellitus, hypercholesterolemia and smoking ( $p > 0.05$  is true form for all variables). Furthermore, the two groups were not significantly different with regard to the coronary arteries grafted during coronary artery bypass surgery ( $P > 0.05$  for all variables). The detection of *C. pneumoniae* IgG positivity underlines the importance of the association between coronary artery disease and *C. pneumoniae*.

**Key words:** Chlamydomphila pneumonia, atherosclerosis, coronary artery bypass surgery.

### INTRODUCTION

Atherosclerosis is a multifactorial process and considered to be an inflammatory disease. Chronic infection may promote arterial inflammation, thereby contributing the initiation or progression of atherosclerosis. *Chlamydomphila*

[*Chlamydia*] *neumoniae* is an obligate intracellular human respiratory pathogen. It has been suggested that coronary atherosclerosis may be an autoimmune process triggered by an infectious agent, most likely *C. pneumoniae*.

**Table 1.** Characteristics of *C. pneumoniae* IgG negative and positive patients.

Characteristic	Total (n = 42)	<i>C. pneumoniae</i> IgG (-) (n = 38)	<i>C. pneumoniae</i> IgG (+) (n = 4)
Age (years)*	65.6 ± 12.0	64.7 ± 11.9	66.5 ± 12.1
Gender (female/male)	14/28	13/25	1/3
HT	27/42	24/38	3/4
DM	16/42	15/38	1/4
Hypercholesterolemia	23/42	21/38	2/4
Smoking	19/42	17/38	2/4
Grafted coronary arteries			
Left anterior descending	42/42	38/38	4/4
Right	32/42	29/38	3/4
Left circumflex	21/42	19/38	2/4

\*Data are presented as mean ± SD. *C. pneumoniae*, *Chlamydomphila pneumoniae*; HT, hypertension; DM, diabetes mellitus.

This atherosclerosis may be an autoimmune process triggered by an infectious agent, most likely *C. pneumoniae*. This proposition is based on the observation of raised antibody titers to *C. pneumoniae* in patients with coronary artery disease in some studies (Saikku et al., 1988; Thom et al., 1991). However, other studies have failed to show seroepidemiological association between infection with *C. pneumoniae* and presence and extent of coronary atherosclerosis (Kark et al., 1997; Weiss et al., 1996). The purpose of the present study was to investigate the effects of coronary artery bypass surgery on *C. pneumoniae* IgG detection in blood samples taken from coronary sinus.

## MATERIALS AND METHODS

Forty-two patients (aged 39 to 83 years) who were consecutive candidates of elective coronary artery bypass surgery for *de novo* lesions (coronary angiography showing ≥70% lumen diameter stenosis in at least one epicardial coronary artery) were enrolled in the study. Patients with acute coronary syndromes, previous myocardial infarction, previous surgical/percutaneous coronary revascularization, active infective disease, ongoing steroid therapy, or connective tissue, pulmonary, renal, hepatic and hematological disorders were not included in the study. Blood samples were drawn from an antecubital vein immediately before the operation and from the coronary sinus during coronary artery bypass surgery. Determination of specific IgG antibodies against *C. pneumoniae* was performed with a commercially available, enzyme-linked immunosorbent assay (ELISA) kit (Vircell, S.L., Santa Fé, Spain) on a fully automated Triturus® ELISA analyzer (Grifols International, S.A., Barcelona, Spain). The IgG cutoff values were defined according to the manufacturer's instructions. The microbiologist was blinded to the clinical status of the patients. Hypertension was described as systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg in at least two separate readings previously diagnosed as hypertension by a physician, or the need for antihypertensive medication. Diabetes mellitus was diagnosed if prior fasting blood glucose level was ≥126 mg/dL on two separate occasions, or if the patient was being treated with insulin or oral antihyperglycemic agents. Hypercholesterolemia was defined as a total blood cholesterol level of ≥200 mg/dL or a low-density lipoprotein-cholesterol

level of ≥130 mg/dL, or using cholesterol-lowering drugs. Smokers were defined as those who had been smoking regularly until admission. Each patient provided informed consent to participate in the study. Continuous variables were expressed as mean ± SD, and categorical variables were expressed as frequencies. Fisher's exact test was used to compare *C. pneumoniae* IgG positivity before and during coronary artery bypass surgery and to compare characteristics of *C. pneumoniae* IgG negative and positive patients. The Mann-Whitney *U* test was used to compare ages of *C. pneumoniae* IgG negative and positive patients. A *P* value of <0.05 denoted statistical significance for all tests.

## RESULTS

This cross-sectional study involved 42 consecutive patients (14 women, 28 men; age = 65.6 ± 12.0 years (Table 1). All patients underwent successful coronary artery bypass surgery. *C. pneumoniae* IgG was negative in all blood samples obtained immediately before coronary artery bypass surgery. In terms of blood samples drawn from the coronary sinus during coronary artery bypass surgery, there were no statistically significant differences between *C. pneumoniae* IgG negative and positive groups with respect to age, gender, hypertension, diabetes mellitus, hypercholesterolemia and smoking (*P* > 0.05 for all variables). Furthermore, the two groups were not significantly different with regard to the coronary arteries grafted during coronary artery bypass surgery (*P* > 0.05 for all variables) (Table 1).

## DISCUSSION

The results of the present study indicate that coronary artery bypass surgery might cause *C. pneumoniae* bacteremia. This finding can be explained by the release of *C. pneumoniae*, which is already present within the atherosclerotic plaque, into the circulation (Kılıç et al., 2012).

Infectious causes for disease with clear inflammatory components, such as cardiovascular disease (Ross et al.,

1993) have long been proposed, but interest in this topic has recently reemerged because of a body of evidence implicating specific infectious agents in the onset and progression of atherosclerosis and related cardiovascular disease (Saikku et al., 1988; Libby et al., 1997; Kiliç et al., 2012). One agent that has attracted particular attention is the obligate intracellular prokaryotic pathogen, *C. pneumoniae*.

The organism has been detected by electron microscopy, immunocytochemistry, direct immunofluorescence and polymerase chain reaction in coronary artery plaque specimens (Campbell et al., 1995; Muhlestein et al., 1996), and it has been cultured from the coronary artery of a patient with coronary artery disease (Ramirez et al., 1996). Attempts to detect endovascular chlamydiae directly in atherosclerotic tissue have produced conflicting results, with positivity rates varying between 0 and 100%; healthy arteries did not contain *C. pneumoniae* (Campbell et al., 1995; Muhlestein et al., 1996; Kuo et al., 1993; Paterson et al., 1998; Ouchi et al., 2000; Yetkin et al., 2002). Detection of *C. pneumoniae* in atherosclerotic tissue with the polymerase chain reaction has been reported to be as high as 84% (Bauriedel et al., 1999). *C. pneumoniae* has been detected in all specimens obtained from the aorta by immunocytochemistry, polymerase chain reaction, electron microscopy and culture methods as well (Juvonen et al., 1997). The relationship between *C. pneumoniae* seropositivity and risk factors for atherosclerosis were investigated by Kiliç et al. (2012). They suggested that in epidemic regions, early diagnosis and specific treatment of *C. pneumoniae* infections may eliminate risk factors for the development of atherosclerosis.

This was a single-center study with a small sample size. Due to strict inclusion criteria for minimizing effects of confounding factors on outcomes, we had to include only a limited number of subjects in stable conditions, presumably not representative of the status of more general populations referred for clinical management. Thus, this unavoidable drawback should be acknowledged in the clinical application of our data.

Consequently, the detection of *C. pneumoniae* IgG positivity underlines the importance of the association between coronary artery disease and *C. pneumoniae*. Our results should stimulate further randomized controlled studies to determine the pathogenic role of this pathogen in the development of atherosclerosis and the prognostic significance of its presence in the atherosclerotic tissue.

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