Gastroduodenal lesions in coronary artery disease patients. *Frequency, endoscopic characteristics and risk factors*

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Helicobacter pylori (*H. pylori*) infection and the use of non-steroidal anti-inflammatory drugs (NSAIDs), especially aspirin, appear to be of overwhelming importance in etiopathogenesis of gastroduodenal (GD) lesions.[1] Therefore, it could be assumed that coronary artery disease (CAD) patients taking low dose aspirin (≤ 325 mg/d), especially in countries with high prevalence of *H. pylori* infection, are at higher risk for GD lesion development. Also, development of GD lesions in these patients would be additionally influenced with some agents with potentially protective [H_2-receptors antagonists - H_2RAs or proton pump inhibitors (PPIs)] or potentially harmful (example, clopidogrel, warfarin, steroids) effect on GD mucosa. The aim of the present study was to assess frequency, endoscopic appearance and risk factors for GD lesions in patients with CAD.

The study was conducted from June 2005 to June 2006 in the Department of Cardiac Surgery, University Hospital Dubrava, Zagreb, Croatia. The 150 patients (109 men; mean age 62.6 ± 10.2 years) with angiographicaly documented CAD were enrolled in the study, regardless of presence or absence of dyspepsia. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the hospital ethic committee. All patients gave their informed consent. Clinical characteristics (age, gender, height, weight, smoking, diabetes, hypertension, hypercholesterolemia), history of previous peptic ulcer disease or erosive gastritis, and chronic medication used until admission (aspirin, NSAIDs, clopidogrel, steroids, H_2RAs, PPIs) were gathered from a structured questionnaire. Chronic use of NSAIDs was defined as ≥3 defined daily doses (DDD) per week, of low-dose aspirin as ≤325 mg per day, clopidogrel as daily dose of 75 mg and of H_2-RAs or PPI as ≥3 DDD per week.

Esophagogastroduodenoscopy (EGDS) was performed in all patients in order to determine the presence of GD lesions and *H. pylori* status. For the purpose of the study, only ulcerations (mucosal defect greater than 5 mm in diameter) and erosions (mucosal breaks of more than 3 mm) were recorded. Biopsy samples were obtained from the antrum (2 samples) and body of the stomach (2 samples), so that lesion could be classified and *H. pylori* detected by staining with hematoxylin and eosin, and according to Giemsa.

The differences between groups were assessed using the non-parametric Student's t test and chi-square test or Fisher's exact test. Independent correlation between aspirin, gender, clopidogrel, H_2RAs, PPIs, NSAIDs, smoking, warfarin and *H. pylori* status (independent variables) and GD lesion (dependent variable) was tested by logistic regression analysis. These results were expressed using a standardized partial regression coefficient ß [Exp (B)] and the corresponding *p* value. The level of statistical significance was defined as $p<0.05$. Esophago-gastroduodenoscopy revealed GD lesion in 88 (58.7%) patients. Gastric erosions were found in 31.3% of patients, while 11.3% of patients had gastric and duodenal erosions, 10.7% had gastric ulcers and 5.3% had duodenal ulcer. Erosions were more frequent than ulcers (42.7% versus 16%) and, altogether, gastric lesions were more frequent than duodenal (53.3% versus 16.7%). The clinical characteristics of the study population are presented in **Table 1**. Patients with GD lesions were more commonly males (79.5% versus 62.9%, $p=0.027$), smokers (36.4% versus 17.7%, $p=0.017$) and PPIs users (40.9% versus 21%, $p=0.013$), while patients with normal endoscopy were more commonly clopidogrel users (33.9% versus 18.2%, $p=0.035$). All patients were using clopidogrel in combination with aspirin. The logistic regression revealed that low-dose aspirin (Exp(B) 17.423, $p<0.001$), smoking (Exp(B) 3.265, $p=0.024$) and H_2-RAs (Exp(B) 5.171, $p=0.044$) independently correlate with GD lesions. Even in combination with aspirin, clopidogrel was not shown to be risk factor for development of GD lesions in our patient (Exp(B) 0.234, $p=0.002$). Consistent with previous report,[2] our study revealed positive endoscopic findings in more than 50% of nonselected CAD patients. Also, as has been previously observed,[2] gastric mucosa was the most common site and erosions were the most common type of GD lesions in CAD patients. Although aspirin dose reduction result in lower frequency of GD lesion and lowest effective dose of aspirin is recommended for patients at high risk for gastrointestinal complications, there is no dose of aspirin efficacious for cardiovascular prophylaxis that also lacks gastrointestinal risk.[3] Even in dose of 10 mg per day or administered infrequently as 81 mg every third day, aspirin significantly lowered the gastric mucosal prostaglandins and caused gastric ulceration.[3] Therefore, it is not surprising that low-dose aspirin use was the most important independent risk factor for GD lesions in our patients. Contrary to aspirin, which inhibits platelet aggregation by irreversibly blocking the enzyme cyclooxygenase essential for synthesis of

thromboxane A_2, clopidogrel produces platelet inhibition by irreversible blocking of adenosine diphosphate (ADP) binding to a purinergic receptor present at the platelet surface.[3] In a randomized, prospective study of the efficacy of clopidogrel given in daily dose of 75 mg as compared with ≤325 mg of aspirin, clopidogrel was marginally more effective than aspirin and resulted in a moderately lower rate of gastrointestinal bleeding.[4] In healthy volunteers clopidogrel caused less GD damage than aspirin given in daily dose of ≤325 mg.[3] Therefore, conventional wisdom suggests that clopidogrel should be a safer, non ulcerogenic alternative for patients at high risk of aspirin-induced ulcers.

On the other hand, it has been reported that combination of clopidogrel and aspirin lead to an increased tendency of GD bleeding.[4] Therefore, it is unexpected that clopidogrel added to aspirin did not increase risk for GD lesion in our patients. However, in the case of dual antiplatelet therapy, excess risk of GD damage seems to be primarily attributed to the dose-dependent ulcerogenic effect of aspirin.[4] In mentioned study, bleeding was higher at the group of patients with highest dose of aspirin (≥200 mg) given alone than in the group of patients treating with clopidogrel in standard dose (75 mg/d) added to lowest dose (≤100 mg) of aspirin.[4] To date, no studies have been compared with the effect of aspirin ≤100 mg/d and clopidogrel in standard dose added to aspirin ≤100 mg/d on GD lesion development. Platelet aggregation plays a critical role in ulcer healing, through the release of various platelet-derived growth factors (PGDF) that promote angiogenesis.[3] Therefore, clopidogrel might not be the primary cause of GD lesion, but its angiogenic effects - inhibition of the release of PGDF through ADP-receptor antagonism - may impair the healing of dose dependent aspirin-induced GD lesion.[3] At the same time, it has been reported that PGDF cause concentration-dependent contraction of aortic strips and is significantly more potent on a molar basis than the classic vasoconstrictor peptide angiotensin II, which has been considered to be the most potent vasopressor agent known.[5] Moreover, PGDF may contribute to the enhanced vasoreactivity of certain atherosclerotic arteries.[5] In the light of these observations, it could be speculated that combination of aspirin in dose ≤100 mg (dose with lower ulcerogenic effect) and clopidogrel lead to better blood supply and enhance the mucosal protective mechanisms, and lowering GD mucosa lesion development risk. It is a possible explanation for less frequency of GD lesion observed in our patients treated with dual antiplatelet therapy. Our findings that the use of H_2RAs was independently correlated with GD lesions is concordant with previous observations that concomitant use of H_2RAs may cover the symptoms of aspirin-related dyspepsia even in the presence of active ulcer.[1] For that reason, H_2RAs was not proven to be for NSAID/aspirin-induced GD lesion prophylaxis.[1] Contrary, several studies demonstrate PPIs to be more effective than H_2RAs supporting use of the PPIs as prophylaxis for NSAID/aspirin-induced GD lesion.[1] Unexpectedly, the results of our study documented that CAD patients with GD lesions used PPIs more frequently than CAD patients with no GD lesions. This fact may be attributed to occasional dyspeptic symptoms that could influence "on-demand" use of PPIs in these patients. However, the occasional "on-demand" use of PPIs due to dyspeptic symptoms probably does not represent the effective prophylaxis of GD lesions. This observation supports the importance of patient's compliance in regular prophylaxis of GD lesions with PPIs that should not rely on symptoms of dyspepsia in patients with CAD using low-dose aspirin.

Our findings that cigarette smoking was associated

Table 1 - Characteristics in coronary artery disease patients with and without gastroduodenal lesion.

Clinical characteristics	Number (%) of patients		
	Lesions 88 (58.7)	**No lesions** 62 (41.3)	***P* value**
Age (years; mean ±_SD)	61.7 ± 11.0	63.9 ± 9.4	0.191
Males	70 (79.5)	39 (62.9)	0.027*
Body mass index (kg/m^2; mean ± SD)	27.8 ± 3.4	27.8 ± 4.1	0.91
Smoking	32 (36.4)	11 (17.7)	0.017*
Aspirin	86 (97.7)	50 (80.6)	0.001*
Mean aspirin dose (mg/d; mean ± SD)	98.8 ± 15.3	99 ± 7.1	0.944
Aspirin and clopidogrel	16 (18.2)	21 (33.9)	0.035*
Warfarin	8 (9.1)	7 (11.3)	0.784
Non-steroidal anti-inflammatory drugs	5 (5.7)	1 (1.6)	0.401
Proton pump inhibitors	36 (40.9)	13 (21)	0.013*
H_2 receptor antagonists	8 (9.1)	4 (6.5)	0.762
Previous erosions	44 (50)	28 (45.2)	0.62
Previous ulcer	22 (25)	11 (17.7)	0.323
H. pylori positive	56 (63.6)	31 (50)	0.13

H. pylori - Helicobacter pylori
*Indicates significant differences

with GD lesion could be explained with the observation that smoking delays GD lesions healing and enhances relapse after healing, affecting adversely the mucosal protective mechanisms.[1] It inhibits mucus secretion, as well as mucosal prostaglandin generation, decreasing mucosal blood flow, inhibiting salivary epidermal growth factor secretion, and inhibiting pancreatic bicarbonate secretion and duodenal mucosal bicarbonate secretion.[1]

Data on whether *H. pylori* contributes to the risk of NSAID-induced GD mucosal injury have been conflicting. Although, the sum of literature reports suggest that *H. pylori* may have a synergistic effect to promote GD lesion in aspirin users[1] our study did not confirm the importance of *H. pylori* in the development of GD lesion in our patients. However, we support the recommendation that *H. pylori* eradication is beneficial in low-dose aspirin consumers with documented peptic ulcer, especially after ulcer bleeding.[1]

Conclusively, our study revealed the occurrence of GD lesions in CAD patients with clinically significant frequency, especially in regard to gastric mucosal lesions. The use of low-dose aspirin was identified as the most important risk factor for GD lesions development. Interestingly, clopidogrel in standard dose (75 mg/d) added to aspirin in dose ≤100 mg/d did not increase risk for GD lesions development. This observation need to be tested for future prospective studies.

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A comparison of the laryngeal mask airway and cuffed oropharyngeal airway during percutaneous dilatational tracheostomy

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Tracheostomy is a standard procedure in critically ill patients requiring mechanical ventilation for prolonged periods, and a percutaneous technique, which has become more widely used, is accepted as an alternative to the surgical approach.[1] In the standard technique of percutaneous dilatational tracheostomy (PDT), the endotracheal tube (ETT) is withdrawn, with the tip of the ETT below, in between, or above the vocal cords. Failure to correctly position the tracheal tube may result in inadvertent puncture of the ETT cuff by the needle or accidental extubation, leading to loss of the airway. In order to decrease the possibility of these complications, the use of a supraglottic airway device such as a laryngeal mask airway (LMA) is suggested during PDT.[2] The cuffed oropharyngeal airway (COPA™; Mallinckrodt Medical, Athlone, Ireland) is a supraglottic airway device consisting of a Guedel shaped airway with a specially designed inflatable high-volume, low-pressure distal cuff, and a proximal 15 mm connector for attachment to the anesthetic breathing system.[3] The COPA is reported to be a reliable airway management in spontaneously breathing or anesthetized patients.[3,4] The use of a fiberoptic bronchoscope (FOB) through the supraglottic devices allows accurate positioning of the catheter into the midline of the trachea, and the visualization of the guidewire running submucosally within the posterior tracheal wall prior to the use of dilator forceps. Also, the COPA may allow fiberoptically guided tracheal intubation via either the oral or nasal route.[5] However, the use of the COPA under fiberoptic visualization to airway control during PDT has not been previously described in the literature. In this study, we aimed to compare the efficiency and safety of the COPA and LMA in airway management during PDT under endoscopic guidance in anesthetized critically ill patients.

This current study was conducted at Uludag University Faculty of Medicine, Bursa, Turkey from December 2003 to January 2005. The PDT was planned in adult patients who need prolonged mechanical ventilatory support in the general intensive care unit (ICU). After Hospital Ethics Committee approval and informed consent from relatives of the patients were obtained, all patients, aged 18-67 years, were randomly assigned to have either the COPA (n=23)