Nasal disorders and cardiovascular damage: flow-mediated dilation and intima-media thickness as risk parameters*

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Dear Editor:

We read with great interest the recent study by YJ Jeon and colleagues which shows the increased risk of cardiovascular diseases in patients with chronic rhinosinusitis (CRS) [(1)]. In the last decades, the relationship between chronic inflammatory disorders and cardiovascular diseases (CVDs) has been widely investigated, since chronic low-grade inflammation has been shown to induce early endothelial dysfunction, which in turn is closely related to the initiation and maintenance of atherosclerosis and, thus, to the increased risk of cardiovascular adverse events [(2,3)]. However, data about the possible correlation between chronic sino-nasal disorders, such as allergic rhinitis (AR), non-allergic rhinitis (NAR), chronic rhinosinusitis with nasal polyposis (CRSwNP), and CVDs are lacking. The authors have finally demonstrated, through a case-control cohort study, the higher prevalence of stroke and ischemic heart disease (IHD) in CRS patients compared with control subjects, even after adjusting for obesity, alcohol consumption, smoking, systolic and diastolic blood pressure, fasting blood glucose, total cholesterol, haemoglobin, and Charlson Comorbidity Index (CCI) scores. Actually, although the mechanisms underlying the involvement of sino-nasal disorders in the increased cardiovascular risk are not yet fully understood, the persisting inflammation of the nasal mucosa could trigger cellular changes and the production of several inflammatory mediators that act on the vascular system and cause pathological alterations [(4)].

In this context, we report our preliminary data which corroborate what YJ Jeon and colleagues have demonstrated. Indeed, assuming the possible involvement of sino-nasal inflammation in the etiopathogenesis of CVDs, we have evaluated early markers of atherosclerosis in 44 patients (31 male, aged between 18 and 68 years, mean age 39.6 years) suffering from sino-nasal disorders (study group) and 42 healthy subjects (control group) (29 male, aged between 17 and 59 years, mean age 32.5 years). In particular, we have assessed the endothelial function using the flow-mediated vasodilatation (FMD) of the brachial artery, according to current recommendations, and the intima-media thickness (IMT) of common right and left carotids, by artery color Doppler ultrasound [(5,6)]. Interestingly, FMD values were abnormal in 68% of patients suffering from sino-nasal disorders, whereas only 21.4% control healthy subjects had FMD abnormal values ($p<0.0001$, OR 7.86). On the other hand, IMT values were within the normal range in both groups, although the mean IMT value was significantly higher in the study group compared to the control group (IMT right: $p=0.022$; IMT left: $p=0,007$) (Table 1). Since the thickening of intima-media appears in a long subclinical period of atherosclerosis, the determination of IMT has emerged as an early indicator of deterioration of the arterial wall. Indeed, several studies have shown that that increased IMT is a useful and reproducible predictor of coronary, cerebrovascular, and peripheral arterial occlusive disease and their complication, as well as a reliable tool for estimation of risk for cardiovascular events [(7)]. Therefore, patients of the study group, although still within normal limits, showed greater thickness of intima-media compared to the control group and consequently a greater risk of CVDs. Similarly, the study group showed abnormal FMD values, which is currently recognized to have a similar predictive ability for cardiovascular disease to traditional risk factors [(8)].

We believe that bringing to light the mechanisms underlying the correlation between chronic sino-nasal inflammation and CVDs is of fundamental importance, since the diagnostic tools and therapeutic strategies available today, including biologic agents, allow to correctly frame rhinological patients and to provide them with tailored and effective treatments [(9)]. This is of paramount importance, with a view not only to treating the sino-nasal disease and improving their quality of life (QoL), but also to prevent the cardiovascular risk, which has been proven to be increased in these patients.

Table 1. Comparison of FMD%, IMT left and IMT right between study group and control group.

	Study group (n= 44)	Control group (n= 42)	P value
FMD, %	6.47	17.47	<0.001
IMT left (mm)	0.70	0.61	0.022
IMT right (mm)	0.87	0.59	0.007

Abbreviations

CVD: Cardiovascular disease; AR: Allergic rhinitis; CCI: Charlson Comorbidity Index; CRS: Chronic Rhinosinusitis; CRSwNP: Chronic Rhinosinusitis with nasal polyps; NAR: Non-allergic rhinitis; QoL: Quality of life; IHD: Ischemic heart disease; FMD: Flow-mediated vasodilatation; IMT: Intima-media thickness

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None

Authorship contribution

MG designed and directed the study and reviewed the final version of the manuscript. RG carried out the bibliographic analysis and wrote the manuscript. ST made the statistical analysis and interpretation of results. LI, KP, NQ, SB, NS, RC, MMC collected data. MC reviewed the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors reported no conflict of interest.

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SUPPLEMENTARY MATERIAL

Materials and Methods

We enrolled 86 consecutive patients at the Departments of Otolaryngology of the University Hospital of Bari and Foggia. The study group included 44 patients, including 31 males (70,45%), suffering from sino-nasal disorders such as allergic rhinitis (AR) 15 (34,1%), non-allergic rhinitis (NAR) 12 (27,3%), chronic rhinosinusitis with nasal polyposis (CRSwNP) 17 (38,7%) (Study group). The age of the patients ranged from 18 to 68 years (median 39.6). The control group included 42 subjects, aged between 7 and 59 years (mean age 32.5 years), with a negative history of sino-nasal disorders, which presented non-obstructing nasal septal deviations (Control group). We carefully examined patients' clinical history, paying greater attention to atopy, presence of asthma, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), and performed endoscopic exams and nasal cytology on all patients, according to validated criteria. Moreover, we assessed the endothelial function of all patients using the flow-mediated vasodilatation (FMD) of the brachial artery, according to current recommendations, and the intima-media thickness (IMT) of common right and left carotids, by artery color Doppler ultrasound.

Statistical analysis was performed using SPSS 25.0 software (SPSS Inc, Evanston, IL). Continuous variables were expressed as mean and standard deviation. Comparison of variables between the different groups was obtained with Student's t test and Chi square test (χ^2). A p value of ≤ 0.05 was considered statistically significant.

Informed written consent was obtained from all participants. The study was approved by the Area 1 Ethics Committee of the University Hospital of Bari and Foggia (number 6854).

Results

The two groups showed similar characteristics with regard to obesity, smoking and hypertension. Supplementary Table 1 shows the median BMI of the two groups as well as the percentage of smokers and patients with arterial hypertension, according to the ESH/ESC guidelines. Therefore, the other results appeared to be independent from these factors.

Supplementary Table 1. Patients.

	Study group	Control group
BMI (median)	25.6	26.1
Smoke habit, %	41%	38%
Arterial hypertension (ESH/ESC Guidelines), %	56%	52%