

Correspondence

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Systemic Inflammation, Atrial Fibrillation, and Cancer

To the Editor:

The article by Chung et al¹ reports a significant elevation of C-reactive protein (CRP) in patients with atrial fibrillation (AF). The CRP elevation was found both in patients with lone arrhythmia and in patients with structural heart disease. Moreover, the higher CRP levels were seen in patients with persistent, rather than paroxysmal, AF.

We recently conducted a study to quantify the clinical observation of an unexpectedly high frequency of AF in patients with colorectal cancer.² We considered a total of 1463 patients admitted to our Department of Surgery from 1987 to 1998 for surgical treatment of colorectal cancer (case group; mean age 66.0 years, 54% males) or nonneoplastic diseases including inguinal hernia, cholelithiasis, varicose veins, and hemorrhoids (control group; mean age 65.6 years, 61% males). We found that atrial fibrillation was three times as likely in patients with first diagnosis of colorectal cancer compared with controls (Mantel-Haenszel sex-adjusted odds ratio=3.5; Cornfield 95% confidence interval=1.6 to 7.2). Logistic analysis was used to exclude an effect of age. All of the patients studied were at the first stage of their diagnosis of colorectal cancer, and they had not received any chemotherapy or previous major surgery.

Different pathophysiological mechanisms could explain our observations: a clinical or subclinical hyperthyroidism related to an abnormal release of thyroid-stimulating hormone or T3-like peptides by the tumor; an imbalance between sympathetic and parasympathetic cardiac autonomic control; an autoimmune paraneoplastic syndrome with inflammatory involvement of atrial structures as antigens.³

Chung et al¹ suggest in their article that AF could be promoted and maintained by atrial structural remodeling because of an inflammatory state, and that elevated CPR may reflect this condition. The cause of the inflammatory state remains unknown.¹ Taking into account the results of our study, the presence of a tumor can sustain systemic inflammation with CPR elevations and could predispose some patients to the development of AF. Moreover, the higher mortality reportedly associated with AF, even after adjustment for preexisting cardiovascular conditions,⁴ could be explained in some of these patients by the presence of an inflammatory state due to an occult neoplasm or other systemic inflammatory diseases.

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1. Chung MK, Martin DO, Sprecher D, et al. C-reactive protein elevation in patients with atrial arrhythmias. *Circulation*. 2001;104:2886–2891.
2. Guzzetti S, Costantino G, Sada S, et al. Colorectal cancer and atrial fibrillation: a case-control study. *Am J Med*. 2002;112:587–588.
3. Maixent JM, Paganelli F, Scaglione J, et al. Antibodies against myosin in sera of patients with idiopathic paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol*. 1998;9:612–617.
4. Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death. The Framingham Heart Study. *Circulation*. 1998; 98:946–952.

Response

The letter of Dr Guzzetti and colleagues reports that the incidence of atrial fibrillation is higher in patients with colorectal cancer. Neoplastic diseases could certainly provide the basis for an inflammatory state that could promote atrial fibrillation. Their study thus offers corroborative evidence linking atrial fibrillation and inflammation. In our study,¹ a history of cancer was reported in 28/202 patients. Cancer was significantly associated with atrial arrhythmias (4/71 [5.6%] of patients without and 24/131 [18.3%] of patients with atrial arrhythmias had history of cancer, $P=0.018$). Cancer was also significantly associated with elevation of C-reactive protein (CRP) levels (0.36 ± 0.06 mg/dL without and 0.51 ± 0.10 mg/dL with history of cancer, nonparametric test $P=0.005$) in univariate analysis. However, multivariate analysis did not identify cancer as an independent predictor of atrial arrhythmias. The finding that cancer was not an independent predictor of atrial arrhythmias after adjusting for CRP levels is consistent with inflammation being the causal intermediary link between cancer and atrial fibrillation.

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1. Chung MK, Martin DO, Sprecher D, et al. C-reactive protein elevation in patients with atrial arrhythmias. *Circulation*. 2001;104:2886–2891.