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REPLY

Auer et al. (1) investigated the relationship between subclinical hyperthyroidism and atrial fibrillation (AF), and they concluded that subclinical hyperthyroidism has a risk of AF. They also speculated that the thyroid hormone may have little effect on the genesis of AF in subclinical hyperthyroidism. We appreciated the comment from Auer and colleagues. However, in the study from Auer et al. (1), 65% of patients with AF were associated with other heart diseases (coronary artery disease, dilated cardiomyopathy and valvular heart disease), and about half of these patients had atrial enlargement. Thus, AF in these patients may be due to the combined effects of thyroid hormone and underlying heart diseases.

Subclinical hyperthyroidism refers to a state with normal thyroid hormone concentrations and low serum thyrotropin concentration. Several causes of subnormal thyrotropin do not reflect the presence of subclinical hyperthyroidism. Serum thyrotropin concentrations are frequently low in patients with severe non-thyroid illness, especially those receiving glucocorticoid. In addition, low serum thyrotropin value may be associated with low or normal serum thyroid hormone in the early stage or shortly after treatment or spontaneous resolution of overt hyperthyroidism (2). In the study from Auer et al. (1), all the patients had underlying thyroid diseases of functional autonomy or autoimmune. It is difficult to diagnose these patients from limited blood samplings, and subclinical hyperthyroidism may be overestimated.

Subclinical hyperthyroidism has been considered to have increasing risk of AF. In the follow-up of 10 years, there was a

threefold relative risk of AF in these patients (3). The negative feedback relationship between serum thyrotropin and thyroid hormone is log linear. Thus, the patients with slight excess of thyroid hormone would have low thyrotropin level, but would have serum thyroxine and tri-iodothyronine concentrations above the mean values for normal subjects but within the normal range. Patients with subclinical hyperthyroidism still have symptoms owing to the biologic effects of thyroid hormone. This means that patients with subclinical hyperthyroidism may still have excess thyroid hormone, and thyroid hormone can induce AF.

Although this experimental hyperthyroidism is not completely similar to usual hyperthyroidism, we investigated the direct effects of thyroid hormone on the electrophysiologic characteristics of pulmonary vein and atrial cardiomyocytes (4). We believe that thyroid hormone increases the arrhythmogenic activity of pulmonary vein cardiomyocytes, which may underlie the occurrence of AF in hyperthyroidism.

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Manifestation of Left Main Coronary Artery Stenosis Is Diffuse ST Depression in Inferior and Precordial Leads on ECG

In the November 1, 2001, issue of the *Journal of the American College of Cardiology*, Yamaji et al. (1) reported on a novel electrocardiographic (ECG) sign for prediction of acute ischemia caused by left main coronary artery obstruction. They found that ST elevation in lead aVR with less ST elevation in lead V₁ is a predictor of left main obstruction. Searching the English-language literature they found only 42 previous reported patients with acute left main stenosis. The ECG description in these studies included right bundle branch block, anterior ST elevation or precordial ST

depression. However, our experience, supported by several studies that were not quoted by Yamaji et al., (1) is that the predominant ECG manifestation of left main stenosis is diffuse ST depression in both the inferior and precordial leads (2-4).

It was shown in both the experimental laboratory and in clinical studies that a sudden obstruction of a left main coronary artery induces an increase of the end diastolic pressure without increasing the end diastolic volume, thus shifting the pressure/volume curve upright (5,6). The sudden increase of the end diastolic pressure reduces the subendocardial coronary flow, resulting in a circumferential subendocardial ischemia (6). The electrical vector is shifted from the epicardium toward the subendocardium, causing diffuse ST depression with inverted T waves in the precordial leads on the surface ECG (2,3,7). Lead aVR faces the cavity of the left ventricle from a right superior axis and thus records a mirror image of the apical leads V₅ and V₆. Hence, if there is ST depression in leads V₅ and V₆, lead aVR will usually show ST elevation. This phenomenon is seen on the ECG in various clinical situations associated with an increase of the left ventricular end diastolic pressure, such as tachycardia-induced ischemia and in chronic infarction with restrictive remodeling (8).

In their study, Yamaji et al. (1) reported on the incidence of ST elevation in each lead, but not on the incidence of ST depression. In two of the three cases reported by Frierson et al. (4) there was ST elevation in lead aVR in addition to marked ST depression in leads V₃ through V₆. In the third case with acute ischemia due to left main stenosis, only mild ST depression was seen in leads V₃ through V₆ and no ST elevation in lead aVR, supporting the concept of lead aVR representing the mirror image of leads V₅ and V₆. Figure 1a of Yamaji et al. (1) shows ST elevation in leads aVR, aVL and V₂, with marked ST depression in the inferior leads. We have previously reported this pattern to represent mid-anterior myocardial infarction (MI) caused by first diagonal branch occlusion (9). In the classic presentation, there is ST elevation in leads I, aVL and V₂, reciprocal ST depression with negative T waves in the inferior leads, and ST depression with tall positive T waves in leads V₄ and V₅ (representing anterior subendocardial ischemia). Four of the eight patients reported in that study had ST elevation in lead aVR in the acute phase and six had ST elevation in lead aVR in the predischARGE ECG. All these patients had an occlusion of the first diagonal branch without stenosis of the left main coronary artery. Thus, it might be that the ECG in Figure 1a presented by Yamaji and colleagues (1) represents ischemia induced by embolization of a thrombus from the left main coronary artery to the first diagonal branch.

It might be that there are cases in which the "reciprocal" ST elevation in lead aVR is more prominent than the ST depression in the leads facing the apex. Previously we reported that "reciprocal" ST depression in lead aVL is seen more often than ST elevation in leads II, III and aVF in the early stages of inferior acute MI (10).

In conclusion, ST elevation in lead aVR is probably a "reciprocal" change to ST depression in leads oriented toward the cardiac apex. Although ST elevation in lead aVR may occur with left main coronary artery occlusion, it may also be detected in other situations with ST depression, such as infarction caused by a first diagonal branch occlusion.

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REPLY

Our series presented all the characteristics of acute myocardial infarction (AMI), including elevated creatine kinase (CK), hemodynamic deterioration, associated with acute left main coronary artery (LMCA) obstruction, not LMCA stenosis (1). Patients in the reports published by Sclarovsky et al. (2,3) showed manifestations of unstable angina. Therefore, we do not believe that 12-lead electrocardiogram (ECG) findings in our patients (LMCA AMI patients) can be compared with findings in their patients (LMCA unstable angina patients). For this reason, our study did not refer to the reports by Sclarovsky et al. (2,3). In our patients, ST-segment depression was found in leads V₅ and V₆ in 38% (6/16) and 44% (7/16) of patients, respectively, whereas lead aVR ST-segment elevation was found in 88% (14/16) of patients. Moreover, lead aVR ST-segment shift was not correlated with