To the Editor:

We read with interest the article recently published by Miyazawa et al in the Circulation Journal, which focused on the association between epicardial fat and smoking status.

Although the association between smoking status and epicardial fat volume appears well substantiated, different and not yet completely understood factors may also play an important role in this context. In detail, we believe that sex hormones appear by far to be a possible additional player underlying such an association.

In a previous study, our group evaluated a cohort of Italian patients diagnosed with metabolic syndrome (MetS). In accordance with the data from Miyazawa et al., we found that smokers displayed increased epicardial fat volume when compared with non-smokers, and smoking was the variable that best predicted epicardial fat volume change ($R^2$ 0.177; $\beta$ 0.453; $P$=0.01).

To test the hypothesis that sex hormones (i.e., testosterone and estrogens) may be involved in the control of regional fat distribution, 1 we evaluated primary prevention in 36 subjects (M/F: 21/15; age: 55±1.5 years) diagnosed with MetS (Monti et al unpublished data). In this study, we found that women displayed higher levels of high-sensitivity C-reactive protein (hs-CRP) than men ($P$=0.002). Interestingly, a strong and positive correlation between epicardial fat obtained from MDCT and hs-CRP was seen in women ($r$=0.426; $P$<0.01) but not in men ($r$=0.142; $P$=0.4). Finally, no differences in epicardial fat volume were detected between premenopausal and postmenopausal women.

This apparent discrepancy might be partly explained by the influence of sex steroids on the metabolic activity of adipose tissue, which leads to different production of pro/anti-inflammatory mediators. Some experimental data suggest an inhibitory effect of estrogens on interleukin-6 gene expression, while an increase in CRP after hormone replacement therapy has also been reported. Of note, the female patients recruited in our study did not have exposure to hormone replacement therapy, making it thus unlikely that such treatment influenced the pro-inflammatory status.

Estrogens may regulate fat mass distribution by preferentially increasing fat accumulation in the gluteofemoral region, but the role of sex-hormones in epicardial fat volume basically still remains unclear. In this context, sex differences have been partly reported by some studies that showed that epicardial fat from female subjects exhibits higher expression of adiponectin and leptin than that of male individuals. Moreover, sex-specific adipose tissue distribution may also result from the production of sex hormones by adipose tissue itself.

Overall, insofar as increased epicardial fat volume is emerging as a hallmark of cardiovascular risk, we believe that further well-designed studies are warranted to elucidate the importance of sex hormones on epicardial fat accumulation and function, as well as the consequences in the pathogenesis of atherosclerosis.

References


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