Another subgroup of the TuMAS men were studied for carotid artery intima-media thickness (IMT), a widely accepted noninvasive measure of preclinical atherosclerosis and a predictor of future adverse cardiovascular and cerebrovascular events. Some previous observations have suggested that carotid IMT may be inversely associated with serum T levels in very old men and in men with type 2 diabetes and obesity. A recent study showed inverse association of serum T with the progression of carotid atherosclerosis in elderly men. We therefore examined the hypothesis that androgen deficiency in ageing men is a risk factor for the development of atherosclerosis and examined the relationship of LOH with cardiovascular risk factors and carotid IMT in a randomly selected subpopulation of 239 men from the TuMAS cohort.

Of the original TuMAS population with LOH, i.e. high symptom score and serum T <9.8 nmol/L, or serum T >9.8 nmol/L but serum LH >6 IU/l (considered compensated or preclinical hypogonadism), 99 had no clinical manifestations of CVD and had not been previously diagnosed with hypertension or diabetes. These men were invited to the study (3 of them were subsequently excluded because of newly diagnosed type 2 diabetes). In addition, another 200 men with a normal T and low LOH symptom score were invited as controls; 140 arrived. Carotid IMT was determined by high-resolution B-mode ultrasound. The hormonal parameters measured were serum T, oestradiol, LH and sex-hormone-binding globulin, while the serum lipid profile was also determined.

We found that both the values of maximum common carotid IMT (1.08±0.34 vs 1.00±0.23 mm; mean±SD) and of maximum IMT of the carotid bulb (1.44±0.48 vs 1.27±0.35 mm) were higher in LOH men than in controls. Carotid IMT was inversely associated with serum T (Figure 3) and the HDL/total cholesterol ratio and it correlated positively with LH (Figure 3), age, blood pressure, BMI, total cholesterol and LDL-cholesterol. In the stepwise multivariate regression model, the independent explanatory variables for carotid IMT were age, total cholesterol, T, LH and smoking. When the group variable for LOH was included in the multivariate model instead of T and LH, the significant explanatory variables for the maximum common carotid ITM were the group variable, age, total cholesterol, T, LH and smoking. When the free androgen index, when substituted for T, was not associated with ITM in the multivariate model.

These results show that hypogonadal status (both absolute and preclinical), along with a high LOH symptom score, is associated with increased carotid artery IMT, providing a marker for subclinical atherosclerosis in middle-aged men. Moreover, T was inversely and LH directly associated with IMT after

Figure 3. Correlations between serum T (left panel) and LH (right panel) and maximum intima-media thickness of the carotid and carotid bulb, respectively, in 236 middle-aged men. From ref. 8, with permission.