having SHT. As shown in Table 3, the two groups displayed similar clinical and biochemical parameters. In particular, no difference was found for circulating thyroid function parameters, alcohol consumption, blood pressure and for heart rate. In addition, the mean period of low serum TSH was super-imposable between patients with diabetes and control group with SHT (1.0±0.7 vs 1.1±0.8 years, respectively). However, when the electrocardiographic measures were compared between the two groups, significant differences were observed. As shown in Figure 1, P wave duration (102.9±7.4 vs. 92.1±5.8 ms, p<0.001), P wave dispersion (13.1±3.4 vs. 7.1±3.5 ms, p<0.001), QTmax (399±18 vs. 388±16 ms, p=0.024), QTmin (341±14 vs. 350±17 ms, p=0.038) and QT dispersion (49.9±9.6 vs. 30.9±9.2 ms, p<0.001) were significantly different in subjects with SHT as compared to patients with diabetes having a low serum TSH while treated with metformin.

DISCUSSION

This study demonstrates that the blunted serum TSH induced by metformin treatment is not associated with changes of electrocardiographic parameters found in patients with real SHT. Indeed, significant differences were found when comparing Pmax, PWD, QTmax, QTmin and QT dispersion between patients with diabetes developing a low serum TSH while treated with metformin and patients with real SHT.

Since the first report by Vigersky R et al6 showing that metformin was able to decrease serum TSH levels in patients with diabetes and hypothyroidism, other studies confirmed this observation.6,8 In contrast, a recent analysis by Diez and Iglesias of a large cohort of patients with diabetes showed no independent and significant relationship between TSH values and metformin treatment in euthyroid patients with diabetes.20 Unfortunately, no data about TSH serum levels before metformin treatment were given; it is thus possible that the TSH levels of patients on metformin could be higher before its introduction. Recently, we have elaborated on this including euthyroid patients with diabetes and borderline high serum TSH levels (>2.5 mU/L) independently of the presence of thyroid antibodies.21

A major question regarding the metformin-induced reduction of serum TSH is whether or not this condition can be considered equivalent to SHT. As in fact suggested by Alevizaki, metformin could prove to be a very efficacious tool to induce TSH suppression without iatrogenic hyperthyroidism effects in thyroid cancer patients.22 Indeed, SHT is defined as a condition of lower than normal serum TSH associated with fT4 and fT3 in the normal range.23 SHT, which may result from endogenous thyroid diseases or exogenous factors, such as L-thyroxine treatment at TSH suppressive doses, is associated with corresponding alterations of the cardiovascular system, including...