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Original Research Article

The role of cardiovascular assessment in low risk thyroid neoplasm patients: results from a tertiary care center experience

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ABSTRACT

Background: After surgery, clinical approach to thyroid neoplasms often involves TSH suppression. An increased cardiovascular (CV) risk due to thyroid hormones excess has already been proved. Aim of the study was to evaluate the role of CV assessment in preventing new events and optimizing the follow-up of these patients.
Methods: After thyroidectomy for low risk thyroid neoplasms, a cohort of 108 women was retrospectively evaluated. A first examination (V1) at the end of primary treatments and a second one (V2) five years later were considered. Clinical and echocardiographic evaluations were performed in each examination. Patients were divided into 3 subclasses depending on TSH-suppression degree in the study period. New cardiovascular events, initiation of new therapies and cardiovascular deaths were recorded.
Results: The incidence of CV events was 7,4%. Patients age (p=0.032), previous CV events (p=0.001), use of lipid-lowering (p=0.002) and antiplatelet (p=0.027) drugs and diabetes mellitus (p=0,049) were associated with total CV events; interventricular septum thickness, BMI and tryglicerides value with ischaemic events (sensitivity 66,6%, 100%, 80%; specificity 91,1%, 55,1%, 77,2%, respectively; p<0.001); TSH-suppression class with arrhythmic events (p=0.035); an increased left ventricular mass index ratio between V2 and V1 with both total (p=0.001) and ischaemic (p=0.002) CV events.
Conclusions: After primary treatments for thyroid neoplasm, a complete CV assessment is advisable in defining TSH-suppression target. Ultrasound parameters appear useful in evaluating CV risk both at baseline and during the follow-up. A periodic revaluation of those parameters may allow the prevention or early diagnosis of new events and complications.

Keywords: Cardiovascular risk, Thyroid cancer, TSH-suppression

INTRODUCTION

After surgery, therapeutic approach to differentiated thyroid carcinoma (DTC) involves an accurate evaluation of the risk of persistence or recurrence of the disease based on histological, clinical and radiological parameters in order to establish the most appropriate subsequent approach: in particular, the necessity and the

entity of TSH suppression are issues to be carefully considered.[1-4]

Due to the very low mortality related to these cancers, especially for those with a low stage of disease at diagnosis, every therapeutic decision should result from a balance between the benefit in preventing recurrences and the related risks, particulary in terms of cardiovascular disease.[5] In these patients, in fact, the incidence of cardiovascular events is increased, particularly in those with a suppressed TSH.[6]

On the other hand, the effects of thyroid hormones on cardiovascular system are well known: the relationship between hyperthyroidsim and atrial fibrillation (AF) has widely been studied both from the physiopathological ponit of view and from the epidemiological one. Even subclinical hyperthyroidism proved association with an increased risk of arrhythmias.[7,8]

TSH exogenous suppression also affects many cardiac function parameters, such as heart rate, blood pression, maximum heart rate, work-load and different kinds of ultrasound findings.[9]

Other data suggest the influence of thyroid axis on coagulation processes, by increasing pro-coagulant factors such as Von Willebrand factor, fibrinogen and factor VIII and reducing anti-coagulant activity of other proteins such as ADAMTS13.[10,11]

Moreover, atherosclerosis seems to be affected by the excess of thyroid hormones.[12]

On these basis, aim of the present study was to investigate the clinical and echocardiographic features of a choort of low risk thyroid neoplasm women and their evolution in time, and to assess the utility of a complete cardiovascular examination at baseline and during the subsequent follow-up. A second goal was to identify clinical, biochemical or ultrasound parameters associated with cardiovascular events, in order to prevent or at least to detect them earlier, so optimizing the care plan for these patients.

METHODS

Subjects

Patients enrolled in this study were female aged over 18 years at the beginning of the study period, who had undergone total thyroidectomy for a nodular thyroid disease, with an available histological report describing a follicular derived, differentiated thyroid neoplasm and with a tumor stage lower than 2. 108 patients were enrolled, the mean age at the time of surgery was 52.7 ±14.7.

A first examination (V1) at the end of primary treatments (surgery and, when necessary, a first dose of radio-iodine therapy), a five years follow-up period and a second examination (V2) at the end of it were retrospectively analysed. V1 had to be performed within 6 months from primary treatments, and a subsequent 5 years follow-up had to be available, unless death due to cardiovascular events.

A written informed consent to join the research was subscribed by all patients before data collection.

From every patient, familiar and personal cardiovascular anamnesis, menopausal and smoking status and the therapeutic scheme administered were investigated. In each examination, body mass index (BMI), blood pressure and heart rate were measured. A blood examination including the thyroid axis (TSH, fT4), thyroglobulin (Tg), anti-thyroperoxidase antiboidies (TPO-Ab), the lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides) and the glycemic one (glycemia, insulin, insulin sensitivity index HOMA and glycosilated hemoglobin) were evaluated. The administered dosage of levothyroxine pro kilogram of body weight (LT4) was annotated. When available, echocardiographic parameters of left ventricular mass indexed to body surface area (LVMI), interventricular septal thickness at end diastole (IVSd), left atrial diameter at end sistole (LAs) and left ventricular ejection fraction (LVEF) were collected.

Subsequent follow-up consisted in clinical, biochemical and ultrasound evaluations performed every six months in our clinic. During the five years considered, the degree of TSH-suppression was assessed dividing the study population in three subgroups: those with no suppression (S0, TSH ≥0.5 mU/l), moderate suppression (S1, 0.1 mU/l <TSH <0.5 mU/l) and severe suppression (S2, TSH 0.1 mU/l).

Lastly, new cardiovascular events or cardiovascular deaths and the initiation of anti-hypertensive, anti-arrhythmic, anti-platelets or lipid-lowering therapies were encounted.

Thyroid neoplasm staging

Thyroid neoplasm stage was assigned after a reclassification of the histologic report according to AJCC/TNM classification, VIII edition, approved since January 1st, 2018.[13]

Biochemical blood tests

Serum thyroglobulin was assayed through immuno-chemiluminescence (Roche Diagnostics, Mannheim, Germany). Functional sensitivity of the method was ≤0.5 µg/l. TSH and fT4 were measured by mean of a ultrasensitive immuno-chemiluminescence methods (Roche Diagnostics). Normality ranges were 0.3-4.2 mIU/l for TSH, 15.4-28.3 pmol/l for fT4. Anti-thyroglobulin antibodies were determined through

commercial assays (DiaSorin, Saluggia, Italia). Automated Roche Modular Analitics E170 were used for serum creatinine (normality range 0.51-0.95 mg/dl), glycemia (65-110 mg/dl), total cholesterol (130-200 mg/dl), HDL-cholesterol (39-60 mg/dl) and triglycerides (40-170 mg/dl) dosage. LDL-cholesterol was calculated by mean of Friedenwald formula.[14] Glycosylated haemoglobin (HbA1c) was dosed by mean of high performance liquid chromatography with TSK gel G7 Variant Hiscolumn (Tosoh Co. Tokyo, Japan), and results were reported in percentage with normality range 4.3–5.8%. Insulin was determined through micro-particle immunoassay (Abbot, Abbot Park, IL, USA): normality range for our laboratory was 2.0–25.0 mU/l.

Echocardiographic exams

Transthoracic echocardiography was performed by means of a Vivid E80 ultrasound machine (GE Healthcare) equipped with a Phased Array probe set at 3.5 mHz. Standard images were obtained with the patient in the lateral decubitus position. LV end-diastolic diameter (LVEDD), posterior wall thickness at end diastole (PWd) and LAs were measured in the parasternal long axis view. LVMI was calculated through the following formula: LV Mass (g)=0.8{1.04 [(LVEDD+IVSd+PWd)3–(LVEDD)3]} +0.6 (21,22) using a dedicated online software (www.csecho.ca)

Statistical analysis

Chi-squared test was used to evaluate the association among non-quantitative or semi-quantitative variables. Quantitative data were correlated by mean of Spearman rank correlation.

Multiple regression test was used for multivariate analysis, considering all variables which had resulted associated at the linear correlation tests. Correlation between non-quantitative and quantitative variables was assessed through logistic regression and cut-off values for the best sensitivity and specificity calculated by mean of ROC curves.

The entity of the variation of each parameter between V1 and V2 was evaluated through Wilcoxon test. The distribution of the variables depending on TSH-suppression class was studied through ANOVA. Kolmogorov-Smirnov test was used to assess data normality.

They are reported in the text as “median, range” if non-parametric, as “mean ± standard deviation” if parametric. Statistical analyses were carried out by mean of MedCalc Portable Launcher software, version 2.2.0.0; the same program was used to create all figures and graphs. Data collection and subsequent analysis were performed in compliance with the Helsinki Declaration, 1964.

RESULTS

Study population

Out of the 108 patients enrolled, eleven (10.1%) had had a previous CV event in their personal history, 35 (32.4%) in familiar anamnesis. Nineteen (17.6%) were active smokers at the time of the first visit, and 13 (12.0%) had stopped smoking since at least one year before.

Seven patients (6.5%) had a diagnosis of diabetes mellitus, 10 (9.3%) were hyperlipidaemic. At the first examination, 36 (33.3%) were in treatment with anti-hypertensive drugs (ACE inhibitors, angiotensin-receptor blockers, beta-blockers, calcium antagonists or diuretics), 12 (11.1%) with lipid-lowering drugs (statins, k-monacolin), 13 (12.0%) with anti-platelets drugs and 12 (11.1%) with estro-progestinic therapy.

Oncological condition

The most represented histology was papillary thyroid cancer (PTC) (88 patients, out of which 80 classical variant and 8 a follicular variant, FvPTC, 4 follicular carcinoma (FTC), in one patient both PTC and FTC were found). Fifteen (13.9%) had a diagnosis of thyroid adenoma. Seventy-seven patients had a stage I, 16 a stage II disease. Seventy-seven patients had been treated with radio-iodine therapy (RAI) (out of which 53 in stage I, 14 in stage II).

A significant association was found between histological type and both RAI execution ($p<0.001$) and RAI dosage ($p=0.007$). A summary of the main population characteristics is reported in Table 1.

Table 1: Summary of study population’s main demographic and clinical characteristics.

Total subjects	108
Age (years)	52,7±14,7
Menopause (y/n)	63/45
Active smokers (y/n)	19/89
Diabetes mellitus (y/n)	7/101
Dyslipidaemia (y/n)	10/98
Previous cv event (y/n)	11/97
Familiarity for heart disease (y/n)	35/73
Anti-hypertensive drug (y/n)	36/72
Lipid-lowering drugs (y/n)	12/96
Anti-platelets drugs (y/n)	13/95
Estro-progestinic drugs (y/n)	12/96
Histology (PTC / FVPTC / FTC / PTC+FTC / FA)	80 / 8 / 4 / 1 / 15
Stage (i / ii)	77/16
Rai (y/n)	77/31
Estro-progestinic drugs (y/n)	12/96

V1: relations among thyroid function tests, echocardiographic and metabolic parameters

At the first examination, administered LT4 dosage, besides the relations with TSH (p=0.002) and fT4 (p<0.001), proved a negative correlation with age (p=0.007), BMI (p<0.001), total cholesterol levels (p=0.045), LDL (p=0.048) and mean blood pressure (p=0.001). It was also positively related to IVSd (p=0.042) and LAs (p=0.005). Only this last association and the one with BMI, however, remained significant at the multivariate analysis (p=0.033 e p=0.005, respectively).

LVMI proved associated with age (p=0.005) and LAs (p=0.001). IVSd was correlated positively with BMI (p=0.011), LAs (p=0.012) and age (p<0.001) and negatively with fT4 (p=0.040) and LT4 (p=0.042). LAs, furthermore, was positively related to age (p=0.015). None of the considered factors correlated with LVEF, and no significant association was found with the initiation of anti-arrhythmic, anti-hypertensive, lipid-lowering or anti-platelet therapy. At multivariate analysis, the only significant correlations were between LVMI and age and between LAs and LT4.

Recurrent and persistent disease

The percentage of biochemical persistent disease (defined as Tg permanently above 1 ng/mL after primary treatments) or recurrent disease (morphological or biochemical) was 6.5%.

It was associated with histological type (p=0.007), and with an administered RAI dosage superior to 110 mCi (sensitivity 100%, specificity 100%, p<0.001).

Tg levels at V1 correlated with the risk of recurrence (p=0.024), although the low sensitivity and specificity at ROC analysis made impossible to define a useful predictive cut-off (cut-off >0.29, sensitivity 100%, specificity 42%, p=0.087).

Incidence of cardiovascular events

Eight cardiovascular events were recorded (7.4%) during the study period, 3 of which were arrhythmic (one atrial tachycardia treated by flecainide, a new onset AF and a AF recurrence), and 5 ischaemic (2 acute myocardial infarction, 2 transient ischaemic attacks and one death due to cardiovascular arrest). We found as predictive elements of total CV and ischaemic events, respectively, the presence of a previous event in personal anamnesis (p=0.001 and p=0.003), the diagnosis of diabetes mellitus (p=0.049 and p=0.012), the use of lipid-lowering (p=0.002 and p=0.004) and anti-platelets drugs (p=0.027 and p=0.007); an important association was also proven with age (p=0.032 and p=0.005) (Figure 1). TSH value at V1 was higher in patients who would develop and ischaemic event (cut-off >0.76 mU/l, sensitivity 100%, specificity 60.2%, p<0.001). In those patients, conversely, administered LT4 dosage was lower LT4 (cut-off ≤1.73 µg/kg/die, sensitivity 100%, specificity 46.9%, p=0.040). Among echocardiographic parameters, only a IVSd > 11 mm proved associated with ischaemic events (sensitivity 66.6%, specificity 91.1%, p<0.001). As regards the metabolic profile, a BMI > 26 kg/m2 and triglycerides > 135 mg/dl showed the same association (sensitivity 100%, specificity 55.1%, p<0.001 and sensitivity 80%, specificity 77.2%, p<0.001, respectively). Out of 8 cardiovascular events, 3 were recorded in the S0 group (2 acute myocardial infarction and a TIA), all the others in the group with severe suppression, S2. TSH suppression class was therefore statistically associated with the incidence of arrhythmic events (p=0.035), although with a very low specificity and positive predictive value (VPN 100%, VPP 6.2%, sensitivity 100%, specificity 52.9%, p<0.001). Limiting this last analysis to those subjects who had not a previous cardiovascular event in their anamnesis, we found that a TSH-suppression ≤ 0,1 mU/l was associated also with cardiovascular event in toto (NPV 100%, PPV 15.2%, sensitivity 100%, specificity 55.6%, p<0.001). On the other hand, TSH-suppression class was not statistically associated with the initiation of anti-arrhythmic drugs (p=0.656), anti-hypertensive (p=0.582), lipid-lowering (p=0.902) or anti-platelets drugs (p=0.543)

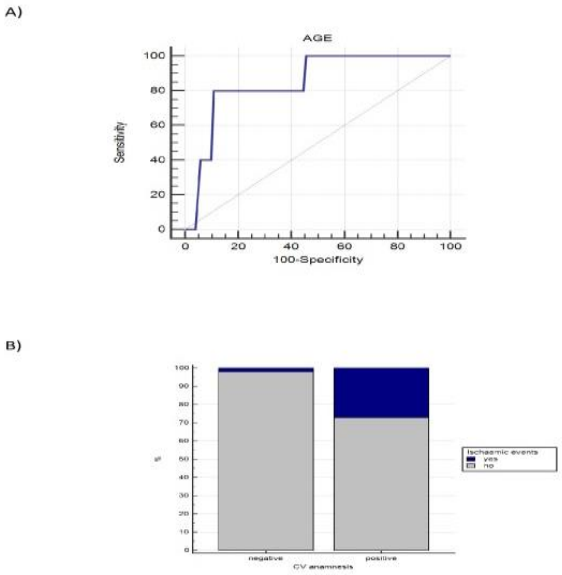

Figure 1: Study of ischaemic events' predictive factors. A) percentage of ischaemic events among patients with positive or negative CV anamnesis: a prevalence of events was seen in the former (p=0.003). B) ROC curve representing the association between age and the incidence of ischaemic events (cut-off >67 years, sensitivity 80%, specificity 89%, p<0.001).

No statistical difference was found between cancer patients and those with a benign pathology report in the incidence of total (p=0.447), ischaemic (p=0.663) and

arrhythmic (p=0.906) CV events. LVMI, LVEF, IVSd and LAs variations from V1 to V2 were not different between the two subgroups, either (p=0.308, p=0.915, p=0.446 and p=0.424, respectively).

Parameters variation between V1 and V2 and the incidence of cardiovascular events

Out of all the variables considered, the only ones that showed a significant difference between the first and the second examination were TSH, fT4 and LT4, which decreased (0.22 vs 0.51 mU/l, p<0.001; 15.3 vs 16.5 pg/ml, p=0.006 and 1.61 vs 1.68 µg/kg/die, p=0.017, respectively), while Tg, TgAb and BMI increased (0.37 vs 0.1 ng/mL, p=0.006; 33 vs 21 U/ml, p<0.001, 26.9 vs 25.4 kg/m2, p=0.014, respectively). At the ROC curve analysis, a significant association was found between the incidence of ischaemic events and TSH ratio (V2/V1) (cut-off ≤ 0.13 mU/l, sensitivity 80%, specificity 75%, p=0.001), LT4 ratio >0.98 (sensitivity 100%, specificity 58.9%, p<0.001) and fT4 ratio ≥1.06 (sensitivity 100%, specificity 73.4%, p<0.001), while an fT4 ratio ≤0.94 was associated with arrhythmic events (sensitivity 100%, specificity 53 %, p=0.035). Among echocardiographic parameters, LVMI ratio between V2 and V1 was associated with total cardiovascular events (cut-off >1.089, sensitivity 100%, specificity 77%, p=0.001). At ANOVA analysis, LVMI ratio proved different depending on TSH-suppression class (p=0.012, Figure 2). None of the other parameters' variation showed association with TSH-suppression class.

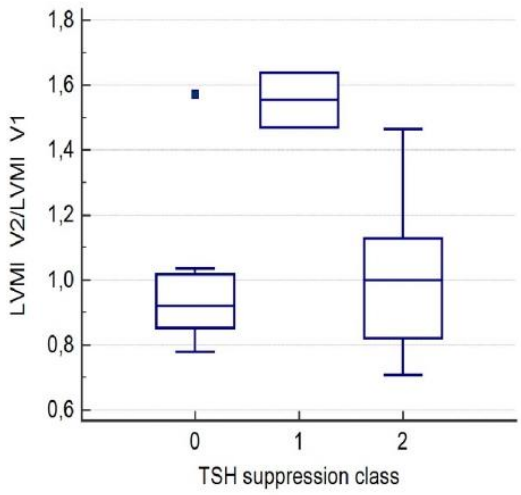

Figure 2: Stratification of LVMI V2/V1 ratio depending on TSH-suppression class during the study period. The largest increase was reported in class 1 (p=0.012).

V2: relations among thyroid function tests, echocardiographic parameters and metabolic profile

Among all the variables considered in V2, TSH levels were correlated not only with fT4 (p<0.001), but also with HOMA index (p=0.043) and negatively with Tg levels (p=0.040) and TgAb (p=0.008). FT4 was correlated with HOMA index (p=0.004), while LT4 dosage was negatively associated with BMI (p<0.001, Fig. 3), HbA1c (p<0.001) and triglycerides (p=0.019). A negative association was also found with LAs (p=0.002) and IVSd (p=0.035), a positive one with HDL (p=0.028).

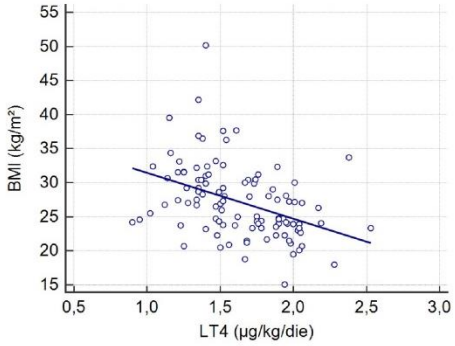

Figure 3: Linear correlation between LT4 dosage (µg pro kilo) and BMI (kg/m2) in V2 (p<0,001).

DISCUSSION

Patients in follow up after DTC show an increased risk of cardiovascular events compared to the population with same demographic characteristics with no history of such disease.[6,15-17]

In the extensive analysis performed by Pajamaki et al in 2017, a significant prevalence of cardiovascular disease was proven in cancer patients, both for the events in toto and for arrhythmic events. The different incidence between cases and controls was much more evident in the younger subgroups of population (<40, 40-60 yrs), that is those in which the "basal" cardiovascular risk was lower.

The risk was also associated with the degree of TSH-suppression and with RAI treatment, although it tended to increase again for TSH value above 0.5 mU/l.[9]

Similarly, in our study population the incidence of ischaemic events proved higher in unsuppressed TSH class than in the moderate-suppression one.

This phenomenon is not surprising since in both cases the study was retrospective, and we also demonstrated the association between a positive cardiovascular anamnesis and the incidence of a new event: patients in secondary prevention, indeed, or those who presented an independently increased risk at the basal examination, did not receive high doses of LT4, also considering the low stage of the oncological disease.

The prediction of CV events in thyroid cancer patients with a negative cardiovascular anamnesis appears more difficult. A recent study conducted by Toulis et al., on the

other hand, proved a higher mortality rate and an higher rate of cerebrovascular events even in those subjects.[15]

This study, even without any data about the degree of TSH suppression, seems consistent with the correlation that we observed between TSH suppression class and the incidence of arrhythmic events, even more significant if restricted to those subjects with no previous events.

In an Israeli study performed on DTC patients compared to a control population matched for age and sex, a significant difference was demonstrated also in the incidence of atherosclerotic events.[16]

Investigating which clinical parameters could predict cardiovascular events, Park et al. defined the 'classical' risk factors (age, sex, obesity, the presence of a previous event) as the most important predictive elements, and these data are consistent with the findings of our study. On the other hand, they also reported an association of cardiovascular outcomes with the stage of the disease, the presence of metastasis and the radio-iodine ablation, which is not present in our data. In our study, on the other hand, we intentionally included only those subjects with a low stage of oncological disease and therefore a lower risk of recurrence: in these patients oncological treatments can be less aggressive and this allows a greater attention to medium-long term cardiovascular outcomes.

A point of interest in the present study, is also the availability of a complete clinical examination of the patients, inclusive of physical parameters, anamnesis, biochemical blood tests and ultrasound assessments: this allowed to evaluate intermediate clinical outcomes besides proper cardiovascular events.

Echocardiographic parameters modification, for example, can be considered as a cardiological outcome itself, which could precede and predispose to the event, and which can take less time to occur than the proper event. In this perspective, the five years follow up considered could suffice to assess cardiological consequences of thyroid neoplasm treatments and may allow to prevent the event itself.

The prognostic role of echocardiographic parameters, indeed, is well established: LVMI proved highly predictive of CV events and death; IVSd and LAs correlate with the incidence of ischaemic and general CV events.[18-21] With specific regard to patients treated for thyroid neoplasms, Wang et al. analysed clinical and echocardiographic parameters in 105 patients treated for DTC and classified according to TSH-suppression and the duration of such condition: in that study they proved significantly different LVEF, time to peak filling from end-systole and heart rate depending on both those elements.[22] In addition, an increased left ventricular mass was proved in TSH-suppressed DTC patients.[23]

Also in the literature review performed by Parker et al. an increased mortality, significant differences in terms of IVSd and an increased ventricular mass were described. Only one of those studies underlined a prevalent diastolic dysfunction in cases compared to the controls.[24]

This last, however, proved altered in other studies, although performed on smaller cohorts of patients: Taillard et al. documented its occurrence even in the early phase of LT4 therapy, and such condition appears often spontaneously reversible once the normal TSH levels are reset.[25,26]

The finding of a negative correlation between LT4 dosage and IVSd is interesting and appears in contrast with data previously reported about thyroid axis and cardiac hypertrophy. Both these parameters, on the other hand, strictly correlate with both age and BMI: after statistical correction for those variables, their correlation was lost.

Conversely, negative correlation between LAs and LT4 dosage persists even at the multivariate analysis, while it loses its significance in V2. A possible interpretation of this phenomenon could be the consideration of the negative effect of hypothyroidism, in this case iatrogenic, on cardiac function, which is reported even at the early stages of subclinical disease.[21]

A matter of discussion could be the larger increase, between V1 and V2, of LVMI in S1 patients than in S2 ones (Figure 2): surely we have to take into account that TSH-suppression is not the only determinant of LVMI variation, which is the result of many different processes; furthermore the low numerosity and the large variability in this subgroup contribute to this statistical finding. On the other hand, the incidence of ischaemic events during the study period proved associated to a higher increase of LVMI, and this confirms the prognostic importance of such parameter and its potential role in the follow-up of this kind of patients.

The effect of LT4 therapy on metabolic profile is debated.[28-35] In our findings, although negative correlations were found between LT4 dosage and total cholesterol, LDL and BMI, at the multivariate analysis only this last remains significant.

In the study published by our group in 2008, lower HDL levels were found in cancer patients than in benign thyroid neoplasm group.[28] Duntas and Brenta in 2012 reported lower LDL in hyperthyroid patients, Lee et al also demonstrated a significant reduction of cholesterol levels in the two years after thyroidectomy.[29,30]

No impairment was found by Heemstra et al., instead, in glycaemic profile and BMI between TSH-suppressed subjects and the controls , and Parker et al didn't prove any difference in glycated haemoglobin and leptin levels between DTC patients and controls.[31,24] On the other

hand, some studies report a higher insulin resistance in hyperthyroid patients.[32]

The relation between thyroid function and body weight is instead well defined: the increase of basal metabolism, resting energy expenditure and thermogenesis induced by thyroid hormones promote the weight loss.[24,32,34,35]

In our study, BMI was found to be negatively related to fT4 and LT4 in V1, and in V2 the relation with LT4 persisted even at the multivariate analysis. No relation between TSH-suppression class and BMI variation was demonstrated, but this last proved negatively related to fT4 and LT4 variations, in line with the findings in V1. On the other hand, a possible explanation of this correlation can be the lower LT4 requirement pro kilo in overweight or obese subjects, due to the lower percentage of lean body mass in these patients: for this reason Ojomo et al suggest that BMI should be taken into account, rather than the simple body weight, in defining LT4 therapy dosage.[36]

With regards to the persistence or recurrence of the disease, a selection bias could be speculated, since only patients affected by low stage of oncological disease were included. This selection was intentionally adopted in order to focus a specific subgroup of patients in which oncological mortality is low. This kind of patients, furthermore, represent the majority of thyroid cancer patients. In these subjects, with a long disease related life expectancy, cardiovascular risk comes out as one of the major concerns. Made these premises, the absence of oncological disease related deaths is in line with literature data according to AJCC VIII for stage I and stage II diseases.[37]

Lastly, a matter of discussion could be the absence of a control group in the present study. That is because we focused on the effects of medium/long-term treatments, especially TSH suppression, regardless the histological report at diagnosis. Patients with less aggressive cancers and benign thyroid neoplasms were then considered together as the “less intensive therapy” subgroup, and compared with the others, more intensively treated. Nevertheless, for a major completeness of the analysis, we also performed a comparison between cancer patients and those with a benign neoplasm report at diagnosis assessing CV events incidence and LVMI, LVEF, IVSd and LAs variation between V1 and V2, and no significant differences were found.

CONCLUSION

In conclusion in DTC patients, and particularly in low risk cases, cardiovascular morbidity and mortality exceed the ones due to their oncological condition. Cardiovascular risk, in these subjects, proved higher than in general population with same demographic characteristics and no history of thyroid neoplasm. This is due to different and complex pathophysiological mechanism, mostly related to supra-physiological doses of LT4 therapy.

A cardiovascular risk evaluation seems therefore necessary both at diagnosis and during the follow-up, and it could be scheduled through a complete baseline assessment.

Particularly, patients presenting a previous cardiovascular event, diabetes mellitus or dyslipidaemia confirmed an increased ischaemic risk and deserve a stricter follow-up, independently from oncological treatments. On the other hand, TSH-suppressed patients show a higher risk of arrhythmic events.

In this regards, echocardiographic parameters such as left ventricular mass index and inter ventricular wall thickness seems useful, easily manageable and predictable of future events, and this make them advisable for baseline and follow-up examinations.

TSH suppression could also play an important role in modifying some of these parameters, possibly predisposing to future events or just altering heart dynamic.

Beside avoiding recurrent or persistent disease, we point out the role of the endocrinologist in preventing cardiovascular complications through a cautious and multidisciplinary follow-up.

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