Anti-Müllerian Hormone Can Help With Predicting Ovarian Failure for Premenopausal Women Who Have Undergone Ablative Radioiodine Treatment for Thyroid Cancer

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Summary

Differentiated thyroid carcinoma is the most common endocrinological malignancy with an increasing incidence over the last 30 years, with women being more frequently affected. In indicated cases, total thyroidectomy followed by adjuvant radioiodine administration is performed, despite current trends towards less aggressive treatment. We would like to investigate the possible adverse effects of radioiodine (RAI) on ovarian function using a simple serum biomarker. Anti-Müllerian hormone (AMH) appears to be the best endocrine marker for assessing physiological age-related oocyte loss for healthy women. The aim of our ongoing prospective study is to determine serum AMH to estimate ovarian reserve for premenopausal women treated with RAI. Over the course of one year, 33 serum samples from women with thyroid cancer and 3 serum samples from healthy women were examined. AMH levels were compared before radioiodine treatment and at regular intervals after treatment. Mean of the AMH level was 5.4 ng/ml (n=33) prior to RAI. The average level of AMH decreased to 1.8 ng/ml in 4-6 months after treatment. In 22.2 % of patients AMH dropped to 0 ng/ml from a non-zero value. Thereafter, we observed an increase in AMH, the average value was 2.7 ng/ml in 8-12 months. We demonstrated a significant decrease in AMH shortly after radioiodine treatment and a subsequent trend of increase at one year after treatment. Consequently, predicting the adverse effects of radioiodine by assessing a serum biomarker could help to select an appropriate treatment strategy for young women planning pregnancy.

Key words

Radioiodine treatment of thyroid cancer • Ovarian reserve • Anti-Müllerian hormone • Premature ovarian failure

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Introduction

Administration of radioactive iodine (radioiodine, RAI, ^{131}I) has been traditionally used to treat thyroid cancer and overactive thyroid for more than 60 years. During this time, its therapeutic effect has been clearly demonstrated for patients with differentiated thyroid cancer at high risk of recurrence to eliminate post-operative thyroid remnants as well as unresectable or incompletely resected thyroid tissue [1]. Thyroid carcinoma has been on the rise worldwide in recent years [2]. It is the fifth most common cancer among the young population (15-39 years), with women being more frequently affected. One-third of women are diagnosed at childbearing age.

Ninety-five percent of thyroid cancers arise from thyroid follicular cells that produce thyroid hormones.

Differentiated thyroid carcinomas (DTCs) are the most common. According to histology, they are divided into papillary (80-85 %) and follicular subtypes (10-15 %) [1]. DTCs are often treated with radioiodine post-operatively because of the cellular specificity for iodine uptake *via* a sodium iodide symporter (NIS). In these cases, the disease has a low mortality rate. Undifferentiated or anaplastic thyroid carcinoma (3 %), and medullary carcinoma from parafollicular C-cells (e.g., as part of MEN2A and MEN2B, 3 %), usually does not respond to RAI due to complete loss of NIS expression [1]. Lymph node and connective tissue tumors (lymphoma, fibrosarcoma, etc., 1 %) are the least represented [3].

The goal of radioiodine therapy is to remove any residual cancer cells and kill the normal thyroid cells remaining after thyroidectomy, resulting in undetectable serum thyroglobulin levels and subsequently improving recurrence-free survival [1]. Although the benefit of radioiodine treatment is distinctly proved for locally aggressive and metastatic cancers, it is controversial for lower-risk cancers. In low-risk ones, the use of radioiodine is on the decline, although established conservative approaches are harder to overcome. There is increasing debate regarding acute and long-term adverse effects. While prospective studies have been conducted for men, there is little data on ovarian reserve in women. It is reported that radioiodine treatment does not affect female fertility [4].

Ovarian reserve is the population of primordial (non-growing) follicles in the ovary [5]. According to its count, reproductive function in premenopausal women can be estimated. Anti-Müllerian hormone (AMH) or Müllerian inhibitory hormone (MIH) is now beginning to be used as one of the main biomarkers of ovarian reserve. Its serum concentration depends linearly on the number of primordial follicles. In relation to radioiodine treatment and its possible adverse effects on reproduction, knowledge of ovarian reserve before treatment will help. Ovarian reserve should be assessed in relation to premature ovarian failure and polycystic ovary syndrome (PCOS). PCOS is a heterogeneous disease and the most common endocrinopathy in women of childbearing age. It affects 4-20 % of women of reproductive age worldwide [6].

Premature ovarian failure occurs due to depletion of the follicular reserve. Extinction of ovarian function with the earlier onset of menopause, typically before the age of 40. Worldwide, it affects 1 % of women and may be iatrogenic induced by effects of gonadotoxic anti-cancer treatments, as well as immunosuppressive drugs, or by surgical interventions in the small pelvis. There is a possible association with autoimmune disease (for example Graves-Basedow thyrotoxicosis, Hashimoto's thyroiditis, type I diabetes mellitus) and/or genetic predisposition and chromosomal abnormalities, including known occurrence in congenital disorders such as Turner syndrome and X chromosome fragmentation syndrome. On the other hand, it can be caused by toxic substances from the environment (smoking, heavy metals, solvents, pesticides).

Determination of ovarian reserve by AMH examination is mainly used for *in vitro* fertilization methods, as well as for prediction of the onset of menopause and thus estimation of the length of the reproductive period [7]. Other indications include diagnosis and monitoring of polycystic ovary syndrome, diagnosis and treatment of granulosa cell tumors of the ovary [8]. It also includes the diagnosis and differential diagnosis of precocious and delayed puberty in boys, diagnosis of cryptorchidism and anorchia in boys, and the differential diagnosis of disturbed sexual development in children [9].

Anti-Müllerian hormone is a glycoprotein dimer with a molecular mass of 140 kDa and a member of the transforming growth factor-β (TGF-β) family. It is encoded on chromosome 19 (19p13.2-13.3). Signalling pathway is transmembrane mediated *via* a dimeric serine/threonine kinase receptor. AMH influences prenatal fetal development and sex differentiation along with other hormonal factors, signalling molecules, and genetic factors (e.g., SF-1 gene, DAX1, SRY) [10]. Under the influence of AMH, the Müllerian ducts regress, thereby inhibiting the development of the uterus, fallopian tubes and upper vagina. In males, AMH is formed in Sertoli cells of the testes most prenatally, from 8-9 weeks after conception, decreases markedly with the onset of puberty as testosterone production increases, and in adulthood the level of AMH remains physiologically low. Compared in female baby, AMH begins forming around 36 weeks of gestation (around the time of birth) in ovarian granulosa cells of growing follicles, peaks around age 25, and continues to decline until menopause [11-12]. AMH is mostly secreted by primary, secondary, preantral and small antral follicles sized <4 mm [12-13]. From the total number of primary oocytes produced ($1\text{-}2\times10^6$), a maximum of 400-500 germ cells are released during the reproductive period, with the remaining germ cells undergoing atresia [14]. Anti-Müllerian hormone is involved in the development of gonads and regulates their

maturation after birth. The main physiological role of AMH is aimed at inhibiting the recruitment of primary follicles, thereby preventing follicular reserve depletion too early – it acts as an antagonist to follicle-stimulating hormone. *In vivo* and *in vitro* experiments have shown that the transition from primary to growing follicles is enhanced in the absence of AMH [15].

Radioactive iodine as a therapeutic drug is used to treat and to identify the main tumor and any metastases. The whole-body scintigraphy followed by RAI administration can detect regional or distant metastases early in the disease, contributing to treatment success and minimizing mortality. After successful ablation of thyroid remnants, we routinely monitor levels of thyroglobulin, a biomarker of viable thyroid tissue, whose rise signals local recurrence or distant metastases [16].

Currently, there is a debate about what should be the smallest amount of radioiodine activity administered to achieve complete elimination of postoperative residues. The German Society of Nuclear Medicine (Die Deutsche Gesellschaft für Nuklearmedizin, DGN) recommends a range of 1-3.7 GBq (about 30-100 mCi) of ^{131}I as the optimal value of ablation activity [17]. Radioiodine treatment is generally well tolerated by patients. However, some short-term and long-term side effects may occur [8]. Temporary side effects include advisory thyroiditis, local swelling of the accumulating residual tissue or metastases, pain, oppression of surrounding structures, gastritis and nausea, sialoadenitis and abnormalities (changes) of taste and smell, and nausea. Depending on the magnitude of activity and cumulative doses administered, bone marrow attenuation, hypospermia and menstrual cycle disturbances may occur. Fertility is reported to be unchanged in both men and women in the long term. While prospective studies have been conducted in men, there is little data on ovarian reserve in women, although fertility is reported to be unchanged [4]. However, the administration of RAI to pregnant and breastfeeding women is strictly prohibited. Long-term side effects can include the development of subsequent secondary malignancies (leukemia and solid tumors), chronic sialoadenitis, taste and smell abnormalities, xerostomia, pulmonary fibrosis, and hypothyroidism [16]. Nevertheless, RAI is considered a safe treatment method thanks to many years of treatment and data from studies.

Information for the publication was obtained and updated by searching PubMed and Medline databases. A local clinical study has been undergoing to determine serum AMH and estimate ovarian reserve for premenopausal women treated with radioiodine at the University Hospital in Hradec Králové. The aim should be to avoid adverse effects of radioisotope therapy for young women with risk factors (e.g., gynecological history of PCOS, endometriosis, fibroids, gynecological tumors, breast cancer, associated internal diseases) and possibly individual consideration of the need for RAI administration. Thus, the justification of the indication, a precise description of the method of treatment, the nature of the disease, the determination of the prognosis and response to treatment.

Patients and Methods

The local prospective study focused on the use of serum AMH determination to estimate ovarian reserve for premenopausal women treated with radioiodine. Within a period of one year (from October 2021 to October 2022), 33 serum samples were previously drawn from women with thyroid carcinoma (18 to <52 years) and 3 serum samples from healthy women (aged 28-35 years) in Hradec Králové, Czech Republic. The average age of the treated group was 35.5 years (n=33). Mean dose of RAI was 4728 MBq. The study has been performed according to the Declaration of Helsinki, the procedure has been approved by the local ethics committee, and informed consent has been obtained from patients. All samples were processed within two hours of collection and stored at -80 °C. Exclusion criteria included history of acute illness within 7 days of collection. Polycystic ovary syndrome was ruled out in the patients after examination of sex hormones including testosterone and on the basis of negative gynecological findings at the beginning of the study. We used the Enzyme-Linked ImmunoSorbent Assay (ELISA) microtiter plates to test the blood samples. The current guidelines have defined the reference interval as two cut-off values within which 95 % of the population falls.

The target group of the study was female patients of childbearing age treated for thyroid cancer. Collection of biological material (venous blood) was performed after informed consent in a selected group of patients. The objectives were gonadotropic axis examination, thyroid function testing and assessment of AMH changes before RAI administration and after RAI administration at regular intervals as per protocol schedule at 3 months, 6 months, 12 months and 18 months after RAI administration. The following were always assessed at each collection: AMH,

gonadotropins and dehydroepiandrosterone, serum proteins with sex hormone binding globulins, thyroid hormones and thyroglobulin with antibodies, basic mineralogram, liver enzymes, screening for type 2 diabetes mellitus, renal function. Patient samples (venous blood) with AMH were continuously accumulated and stored by freezing for subsequent AMH measurement by ELISA (one AMH Gen II ELISA kit designed to test 80 samples by sandwich detection). The control group consisted of 3 healthy female patients with a comparison of AMH and gonadotropic axis function at an interval of one year. The list of analytes investigated is clearly summarized in Table 1.

Table 1. Laboratory protocol.

Sexual hormones	Thyroid hormones	Proteins	Mineralogram	Liver enzymes	Renal functions	Diabetology screening
AMH, E2, FSH, LH, P, PRL, hCG, DHEA, FRTST, TTST	T3, FT3, T4, FT4, Tg, TgAb	SHBG, TP, A	Na^+, K^+, Cl^-	ALT, AST, ALP, GGT	Urea, creatinine	Fasting glycaemia, glycated hemoglobin (HbA1c)

AMH: anti-Müllerian hormone; E2: estradiol; FSH: follicle-stimulating hormone; LH: luteinizing hormone; P: progesterone; PRL: prolactin; hCG: human chorionic gonadotropin; DHEA: dehydroepiandrosterone; FRTST: testosterone free; TTST: total testosterone; T3: triiodothyronine; FT3: free triiodothyronine; T4: thyroxine; FT4: free thyroxine; Tg: thyroglobulin; TgAb: anti-thyroglobulin antibodies; SHBG: sex hormone binding globulin; Na^+: Sodium; K^+: Potassium; Cl^-: Chloride; ALT: alanine transaminase; AST: aspartate transaminase; ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; HbA1c: glycated hemoglobin.

Calculation of organ doses (ovaries) and calculation of applied ^{131}I activities administered to patients for ^{131}I radioiodine therapy was performed in Dosewatch software from GE Healthcare according to the Local Radiological Standards of the Department of Nuclear Medicine of the University Hospital Hradec Králové. Microsoft Excel spreadsheet, which is a part of Microsoft Office software, was used for statistical processing. The results of the analysis were correlated with data obtained using conventional standard methods. The reference range of AMH levels was determined by the ELISA kit manufacturer (Beckman Coulter, Czech Republic). The calculated standardized absorbed dose according to the 2014 International Commission on Radiological Protection Recommendation (ICRP Publication 128) in the ovary for the reference patient is 0.036 mGy/MBq. The Ethics Committee of the University Hospital Hradec Králové expressed its approval of the proposed clinical trial.

In the AMH kit (Beckman Coulter, Czech Republic) available in our hospital laboratory, the measurement range is 0.05-22.5 ng/ml. The established limit for AMH is 1.3-5 ng/ml, but this limit applies to *in vitro* fertilization. AMH reaches its highest values in the reproductive period, peaks around age 25, then it gradually declines until menopause. A normal concentration of AMH in the serum indicates a sufficient number of ovarian eggs and thus optimal fertility. For healthy women, circulating AMH levels correlate directly with primordial follicle counts (=gonocytes surrounded by a single layer of flat cells) [5]. Low levels of anti-Müllerian hormone (AMH<0.5 ng/ml), estradiol (E2<20 pg/ml), as well as a decrease in inhibin B and an increase in gonadotropins (follicle-stimulating hormone, FSH>40 IU/l) are conclusive markers for the diagnosis of ovarian depletion [19]. AMH is considered an excellent marker of ovarian reserve due to the stability of its serum levels and the possibility of determination without affecting the result at any stage of the menstrual cycle [20].

Interpretation of serum AMH levels varies according to laboratory standards and thresholds. AMH is found in the serum in the inactive unsplit form of pro-AMH and the split, biologically active form of AMH (AMHN, AMHC). The biologically active molecule consists of two N-terminal and two C-terminal non-covalently coupled fragments that bind to the AMH type 2 receptor (AMHR2). Pro-AMH and AMH (AMHN, AMHC) are detected immunologically [12]. ELISA sandwich detection method uses capture and detection antibodies that bind to the N- and C-terminal parts of AMH.

Treatment of thyroid carcinomas with radioiodine is usually performed in hospital over a 7-day hospital stay. The general management of thyroid cancer is recorded in Table 2. Table 3 describes the

Table 2. RAI therapy of thyroid carcinomas.

Therapeutic procedure	Comment
1. Surgical removal of the thyroid gland – hemithyroidectomy or total thyroidectomy according to the risk – histological variant and grade of the carcinoma, clinical stage.	Differentiated carcinomas: follicular, papillary, oncocytic (recognized as a separate entity or as a variant of follicular carcinoma); undifferentiated carcinomas: medullary, anaplastic; microcarcinoma – a tumor up to 20 mm in the largest diameter (previously up to 10 mm).
2. Thyroid-stimulating hormone (TSH) suppressive thyroid hormone therapy or subsequent radioiodine therapy to destroy postoperative residues – only relevant for tumors with the ability to uptake/accumulate radioiodine.	Repeatedly administration of RAI – in a case of early detected local recurrence of cancer – without/with metastatic lymph node involvement, if there is no indication for surgical removal; multiple administrations are possible, usually in a higher dose of RAI, then we add the applications, i.e., cumulative dose; loss of the ability to uptake radioiodine after repeated applications and with carcinoma dedifferentiation.
3. Follow-up at regular intervals in the Nuclear Medicine Department – regular laboratory checks, neck ultrasound, ^{99}Tc-MIBI scintigraphy.	Laboratory marker of recurrence: thyroglobulin, therapeutic target – suppression of TSH.

Table 3. Treatment with radioiodine.

Course of hospitalization and radioiodine treatment
First day – 1. ultrasound of thyroid, 2. initial laboratory collections (blood count, basic mineralogram, liver and kidney function), 3. administration of small dose of radioiodine for thyroid scintigraphy (24-hour accumulation test), 4. intramuscular injection of Thyrogen in some cases. **Second day** – 1. thyroid scintigraphy, 2. administration of radioiodine at 12 am, 3. intramuscular injection of Thyrogen in some cases. **Third day** – administration of radioiodine at 12 am for patients with Thyrogen addition. 42 h after the radioiodine administration, we usually start thyroid hormone replacement at a supratherapeutic dose; the aim is also to suppress the stimulatory effect of TSH on any residual tissue. Whole-body scintigraphy with radioiodine is performed 6 days after treatment – to detect metastatic lymph node involvement, evaluate residuals and predict possible further radioiodine administration, usually 6-12 months apart. After RAI treatment, the patient is regularly monitored by laboratory and clinical examination at intervals of 6 weeks, 3 months, 6 months, 12 months, 18 months after the radioiodine administration, then every 6 months, after setting the replacement dose of thyroxine, once a year, the checks include neck ultrasound and in case of positive post-therapy scintigraphy also once a year ^{99}Tc-MIBI, ^{18}F-FDG-PET/CT of the trunk.

Dose of radioiodine for patients is calculated by clinical-empirical method. (The 4th Department of Internal Medicine – Hematology, University Hospital Hradec Králové).

treatment of thyroid cancer at The 4th Department of Internal Medicine – Hematology, University Hospital Hradec Králové. The indicated patients are men and women over 18 years of age, the upper age limit is not limited, except for patients contraindicated for treatment, the very old, comorbid and uncooperative persons. However, we have the option of treatment with the addition of Thyrogen. Thyrogen is recombinant TSH and is applicated intramuscularly in 2 doses over two days to patients with postoperative thyroxine replacement, indicated in cases at risk of long-term hypothyroidism (elderly patients with comorbidities, prognostically worse

Table 4. Results of prospective study.

Prospective study – preliminary results
The average age of the whole group: 35.5 years (n=33)
Mean dose of RAI: 4728 MBq
Mean equivalent RAI dose to the ovaries: 175 mGy
AMH level mean, 1. blood draw before RAI therapy: 5.4 ng/ml (n=33)
AMH level mean, 2. blood draw 4-6 months after RAI therapy: 1.8 ng/ml (n=18)
AMH level mean, 3. blood draw 6-8 months after RAI therapy: 2.7 ng/ml (n=6)

Research results at The 4th Department of Internal Medicine – Hematology, University Hospital Hradec Králové.

thyroid cancer variants requiring early postoperative TSH suppression).

Results

In the test group (n=33), mean of the AMH level was found to be 5.4 ng/ml before radioiodine treatment. 18 women were compared with 2 AMH collections and 6 women with 3 AMH collections after radioiodine treatment. In the second sampling 46 months after RAI treatment, the AMH level decreased significantly, with an average AMH value of 1.8 ng/ml (n=18). 22.2 % of patients experienced a decrease in AMH level to 0 ng/ml from non-zero levels 4-6 months after RA treatment (n=18). Subsequently, in the third blood sampling 6-8 months after RAI treatment, the AMH level increased slightly to an average AMH level of 2.7 ng/ml (n=6). Equivalent (absorbed) dose of radioiodine to the ovaries was calculated, with an average of 175 mGy in the treated group**.** Clinically minor variations in the regularity of the menstrual cycle occurred in all cases. Very low AMH levels at the beginning of treatment, as well as after radioiodine administration, were observed in women aged about 50 years. The results are summarized in Table 4.

Discussion

Differentiated thyroid carcinoma is the most common endocrinological malignancy with an increasing incidence over the last 30 years. It is the fifth most common cancer in the young population (15-39 years). DTC is generally diagnosed in females aged 30-39 years. Differentiated papillary and follicular carcinomas account for the highest proportion of all thyroid carcinomas. Surgical removal of the tumor is the standard treatment method. In indicated cases, adjuvant administration of radioiodine follows. An excellent prognosis for survival of differentiated carcinomas is documented. The five-year survival rate is close to 100 % for localized disease and 96 % reported for locoregional disease with metastatic lymph node involvement. Total thyroidectomy followed by RAI is recommended for all patients with DTC>1 cm, despite international trends for less aggressive treatment.

Studies addressing the adverse effects of RAI on ovarian function and female fertility are available from the literature. Measurement of serum anti-Müllerian hormone levels was used as a possible predictor of ovarian reserve. The studies were designed to compare AMH levels before RAI and one year after RAI and pregnancy rates in thyroid cancer patients receiving RAI therapy compared with thyroid cancer patients not receiving RAI. For normoovulatory women, a positive correlation was found between serum AMH levels and antral follicle count (AFC) ($R=0.6$, $P<0.0001$) [21]. Also, this correlation confirmed in the study of Barbakadze *et al.* and has a predictive value for women undergoing *in vitro* fertilization or ovarian hyperstimulation, to estimate the acquisition of sufficient ovarian eggs [22]. AFC (2 to 10 mm in both ovaries) in the early follicular phase correlates with ovarian reserve and low AFC is a sign of ovarian aging [23].

Examination of AMH has become increasingly important in current clinical practice. International studies have reported AMH as the best endocrine marker to assess physiological age-related oocyte loss for healthy women. The effects of RAI on AMH levels were more significantly observed for patients over 35 years of age. Although meta-analyses of data from retrospective studies show a significant decrease in AMH levels after radioiodine therapy of DTCs, there was no evidence of a long-term decrease in pregnancy rates. Table 5 documents the summary of results from retrospective studies. However, further prospective studies with more

Table 5. Results of 22 retrospective studies.

Retrospective studies of RAI treatment
Mean administered radioiodine activity: 3700 MBq (1110-40700 MBq).
Changes observed in the first year after RAI treatment by frequency: menstrual cycle irregularity (12-31 % of patients), amenorrhea (8-16 %).
Earlier onset of menopause (49.5 years) compared to women without radiation exposure (51 years) [29].
Mean AMH concentration after RAI treatment was 1.79 ng/ml (performed in 7 studies).
Mean difference in AMH concentrations before RAI treatment and after RAI treatment (assessed in 4 studies): 1.5 ng/ml (but no reduced risk of pregnancy).
Dependence on the choice of population cohort and consideration of risk factors that may significantly influence data – infertility, active malignancy and gonadotoxic therapy – study of the relationship between serum AMH levels and follicle density (AFC), obesity and metabolic syndrome [22,30].
The results of the prospective studies conducted to date are from testing a small number of patients over a short period of time, and the majority of patients enrolled did not receive high doses (range 1110 to 5550 MBq) or did not receive repeated treatment [29].

data should be conducted to verify these results. In relation to reproductive disorders, calculations of ovarian absorbed doses of radioiodine for patients after thyroid cancer therapy have not been performed yet. We must consider the physiological decline over time with the age of the woman.

AMH as a fertility marker is not used alone. Minimal assessment of AMH, follicle-stimulating hormone, estradiol and inhibin B is established. Variations in serum AMH levels may be due to the action of various factors including combinations of factors (e.g., intra-individual differences, age, body constitution, genetic factors, race/ethnicity, associated diseases, drug therapy) that have not been adequately investigated [24]. Despite this, AMH appears to be a unique endocrine parameter in the investigation of ovarian reserve. Indeed, levels of AMH are stable at any stage of the menstrual cycle, are not affected by the use of oral contraceptives, and even do not change during pregnancy, when the release of endogenous gonadotropins is substantially reduced. These findings are consistent with the idea that AMH levels reflect continuous FSH independent non-cyclical growth of small follicles in the ovary [20]. It is known that as a woman ages, AMH gradually decreases to unmeasurable values, reflecting the number of remaining follicles in the ovary. The exception is polycystic ovarian syndrome (PCOS), where higher AMH concentrations can be detected even for older women. Other variation in AMH levels caused by hypothyroidism, may be one of the risk factors and reasons for poorer reproductive outcomes [25]. Previous studies show that thyrotropin (TSH) and thyroid hormones act directly on the ovary through binding to specific receptors which presence involve in the proper course of folliculogenesis and ovulation [26].

Conclusions

AMH has gained interest as a possible predictor of ovarian reserve in recent years. We demonstrated a significant decrease in AMH levels 4-6 months after radioiodine treatment and a subsequent slight increase one year after treatment. Despite this, the question of possible side effects of radioiodine remains open and therefore the need to inform patients undergoing this treatment. Consequently, predicting the adverse effects of radioiodine by assessing a simple serum biomarker could help to select an appropriate treatment strategy for young women planning pregnancy.

Conflict of Interest

There is no conflict of interest.

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