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RESEARCH ARTICLE

Effect of Radioactive Iodine Ablation Therapy on Ovarian Reserve in Patients with Differentiated Thyroid Cancer

Diferansiye Tiroid Kanserli Hastalarda Radioaktif İyot Ablasyon Tedavisinin Ovaryan Rezerve Etkisi

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ABSTRACT

Objective: Radioactive iodine (RAI) ablation therapy is widely used in the management of differentiated thyroid cancer (DTC). However, its potential adverse effects on ovarian reserve in premenopausal women remain an important clinical concern. This study aimed to investigate the association between RAI ablation therapy and ovarian reserve in premenopausal patients with differentiated thyroid cancer.

Materials and Methods: This study included 66 premenopausal women aged 18–45 years with DTC. Among these patients, 46 received RAI therapy and 20 did not. Serum anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), and thyroid-stimulating hormone (TSH) levels were measured. To evaluate in-dependent association between RAI therapy and ovarian reserve, a multivariable linear regres-sion analysis was performed with AMH as the dependent variable.

Results: AMH levels were significantly lower in patients who received RAI therapy compa-red with those who did not (1.34 ± 0.37 ng/mL vs 1.79 ± 0.25 ng/mL, p = 0.001). No signifi-cant differences were observed between the groups in serum FSH, LH, or E2 levels. AMH levels did not differ significantly according to RAI dose categories of 75, 100, and 150 mCi (p = 0.073). In the multivariable linear regression analysis, RAI therapy remained indepen-dently associated with lower AMH levels (β = −0.41, p = 0.003). Age was also independently associated with AMH levels (β = −0.36, p = 0.010).

Conclusion: RAI therapy was associated with lower AMH levels in premenopausal women with DTC, suggesting a potential adverse effect on ovarian reserve. Larger prospective studies are needed to confirm these findings.

Keywords: Differentiated thyroid cancer, radioactive iodine, ovarian reserve, anti-Müllerian hormone.

ÖZET

Amaç: Radyoaktif iyot (RAI) ablasyon tedavisi, diferansiye tiroid kanseri (DTK) yönetimin-de yaygın olarak kullanılmaktadır. Bununla birlikte, premonopoz kadınlarda over rezervi üze-rindeki olumsuz etkileri klinik endişe oluşturmaktadır. Bu çalışmada, RAI ablasyon tedavisinin premenopozal DTK hastalarında over rezervi ile ilişkisini araştırmayı amaçladık.

Gereç ve Yöntemler: Bu çalışmaya, 18–45 yaş aralığında 66 premenopozal DTK hastası dahil edildi. Hastaların 46'sı RAI tedavisi almış, 20'si ise almamıştı. Serum anti-Müllerian hormon (AMH), folikül stimülan hormon (FSH), luteinizan hormon (LH), östradiol (E2) ve tiroid sti-mülan hormon (TSH) düzeyleri ölçüldü. RAI tedavisi ile over rezervi arasındaki bağımsız iliş-kiyi değerlendirmek amacıyla, bağımlı değişken olarak AMH düzeyinin alındığı çok değişkenli doğrusal regresyon analizi yapıldı.

Bulgular: AMH düzeyi, RAI tedavisi alan hastalarda almayanlara göre anlamlı derecede daha düşüktü (1.34 ± 0.37 ng/mL'ye karşı 1.79 ± 0.25 ng/mL, p = 0.001). Gruplar arasında serum FSH, LH ve E2 düzeyleri açısından anlamlı fark saptanmadı. AMH düzeyleri, 75, 100 ve 150 mCi RAI doz gruplarına göre anlamlı farklılık göstermedi (p = 0.073). Çok değişkenli doğrusal regresyon analizinde, RAI tedavisi daha düşük AMH düzeyleri ile bağımsız olarak ilişkili bu-lundu (β = −0.41, p = 0.003). Yaş da AMH düzeyi ile bağımsız olarak ilişkiliydi (β = −0.36, p = 0.010).

Sonuç: Premenopozal DTK hastalarında RAI tedavisi, daha düşük AMH düzeyleri ile ilişkili bulundu ve bu durum over rezervi üzerinde olası olumsuz bir etkiye işaret etmektedir. Bu bul-guların doğrulanması için daha geniş prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Diferansiye tiroid kanseri, radyoaktif iyot, over rezervi, anti-Müllerian hormon.

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INTRODUCTION

Although thyroid cancers constitute less than 2% of all cancers worldwide, they represent the most common endocrine malignancy. According to a study conducted by the Turkish Public Health Institute Cancer Department in 2020, thyroid cancer was the second most common cancer among women and the ninth most common among men. Differentiated thyroid carcinomas (DTC) account for 92.2% of all thyroid cancers (papillary carcinoma 82.2%, follicular carcinoma 6.1% and Hürthle cell carcinoma 3.9%) (1,2). Radioactive iodine (RAI) ablation therapy is widely used in patients diagnosed with differentiated thyroid cancer to reduce the risk of recurrence by ablating residual thyroid tissue after surgery. In addition, RAI is used to treat unknown or suspected metastatic diseases. RAI ablation therapy has been associated with a statistically significant increase in secondary malignancies. In particular, when the total RAI dose exceeds 500–600 mCi, the risk of leukemia and solid organ tumors increases significantly. In addition to the risk of malignancy, RAI ablation therapy may cause sialadenitis, dry mouth, dental caries, and nasolacrimal duct stenosis. Moreover, RAI ablation therapy may adversely affect the male and female gonads (3).

Anti-Müllerian hormone is secreted by granulosa cells of primary and preantral ovarian follicles and is considered one of the most reliable biomarkers of ovarian reserve. In addition, follicle-stimulating hormone, luteinizing hormone, and estradiol are key reproductive hormones regulated by the hypothalamic–pituitary–gonadal axis and are frequently used to evaluate ovarian function (4). In this study, we aimed to investigate the effects of radioactive iodine ablation therapy on the ovarian reserve in patients with differentiated thyroid cancer.

MATERIALS AND METHODS

This case–control analytical study evaluated the effect of RAI ablation therapy on the ovarian reserve in patients with well-differentiated thyroid cancer. The study included 46 patients aged 18–45 years who received RAI treatment and 20 patients who did not receive RAI treatment, all of whom had been diagnosed with differentiated thyroid cancer and presented to the Endocrine Diseases Outpatient Clinic of Yüzüncü Yıl University between February 1, 2019, and June 30, 2019. The exclusion criteria were as follows: refusal to participate in the study, age <18 or >45 years, use of oral contraceptive drugs, diagnosis of polycystic ovary syndrome, diagnosis of diabetes mellitus, history of oophorectomy, infertility, and presence of an active malignancy. Ethical approval for the study was obtained from the Yüzüncü Yıl University Non-Drug and Non-Medical Device Research Ethics Committee before the initiation of the study (date: November 13, 2018, decision number: 3). During the implementation phase, patients were informed about the purpose of the study and written and verbal informed consent was obtained from those who agreed to participate.

This study was financially supported by the Scientific Research Projects Coordination Unit of Yüzüncü Yıl University (Project No: TTU-2019-8096). Patients who agreed to participate were asked about their age, height, weight, age at menarche, number of children prior to RAI therapy (if applicable), menstrual status after RAI therapy, and number of children after RAI therapy. In addition, patients' medical records were retrospectively reviewed to obtain tumor size, administered RAI dose, and date of RAI ablation therapy. Anthropometric measurements were obtained by measuring the height and body weight. The body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). BMI was classified as underweight (<18.50 kg/m^2), normal weight (18.50–24.99 kg/m^2), overweight (25.0–29.99 kg/m^2), or obese (≥30.0 kg/m^2).

At the time of routine outpatient blood sampling, a single 3-mL blood sample was additionally obtained from each patient and placed into dry biochemistry tubes without an anticoagulant. Samples were centrifuged at 3500 rpm for 10 minutes, and the serum was aliquoted into 1-mL Eppendorf tubes and stored at −80°C until analysis. The reference ranges used were as follows: TSH 0.57–4.2 µIU/mL, FSH 0–12.4 mIU/mL, LH 0–8.6 mIU/mL, estradiol (E2) 21–251 pg/mL, and AMH 0.08–20 ng/mL. Serum FSH and E2 levels were measured using the chemiluminescent microparticle immunoassay (CMIA) method on an Abbott Architect ci16200 autoanalyzer in the hospital's biochemistry laboratory. The serum FSH levels were expressed in mIU/mL, while the serum E2 levels were expressed in pg/mL. Serum LH levels were measured using CMIA on an Abbott Architect i2000 autoanalyzer and expressed in mIU/mL. Serum AMH levels were measured using the enzyme-linked immunosorbent assay (ELISA) method on a Biotek Instruments ELx800 reader. AMH concentrations were expressed in ng/mL (Table 1). For the AMH assay, 50 µL of standard was added to nine wells starting from the second column, followed by 50 µL of streptavidin-Horseradish Peroxidase (HRP). For sample wells, 40 µL of sample, 10 µL of AMH antibody 1, and 50 µL of streptavidin-HRP were added (Figure 1). The plate was gently shaken, covered, and incubated at 37°C for 60 minutes. After incubation, the wells were washed five times with washing solution prepared by diluting the wash buffer 30-fold with distilled water (250 mL). After washing, 50 µL of Chromogen Reagent A and 50 µL of Chromogen Reagent B were added to each well and incubated at 37°C for 10 minutes. The reaction was stopped by adding 50 µL of stop solution to each well (Figure 2). Absorbance was measured at 450 nm. A standard curve was generated using CurveExpert 1.4 software based on standard concentrations and optical densities, and sample concentrations were calculated accordingly.

To account for potential confounding factors affecting ovarian reserve, a multivariable linear regression analysis was performed with AMH as the dependent variable. Independent variables included age, body mass index (BMI), TSH level, tumor diameter, and time elapsed since RAI therapy. Variables that were clinically relevant or showed potential association in univariate analyses were included in the model. All data were entered into the Statistical Package for the Social Sciences (SPSS) version 22.0 software. Descriptive statistics were expressed as frequencies, percentages, means, standard deviations, and minimum and maximum values. Normality of

Table 1. Standard solutions for AMH were prepared

Standard no	Concentration	Process
Standard no:5	12 ng/ml	120 µl original standart + 120 µl standart dilution
Standard no:4	6 ng/ml	120 µl standart no: 5 + 120 µl standart dilution
Standard no:3	3 ng/ml	120 µl standart no: 4 + 120 µl standart dilution
Standard no:2	1.5 ng/ml	120 µl standart no: 3 + 120 µl standart dilution
Standard no:1	0.75 ng/ml	120 µl standart no: 2 + 120 µl standart dilution

Figure 1. Appearance of the plate after adding the sample, antibody and Streptavidin HRP

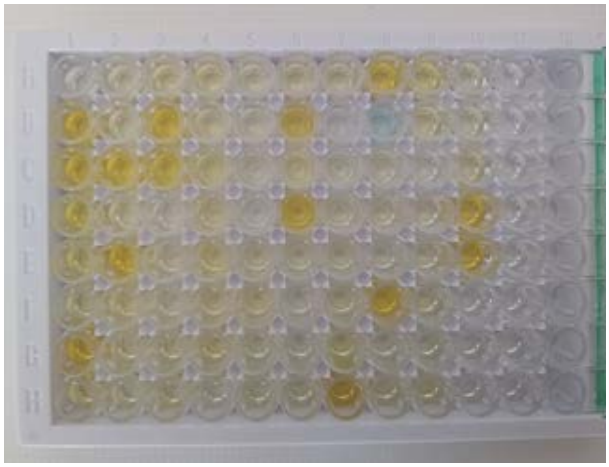

Figure 2. Appearance of the plate after adding the stop solution

continuous variables was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Variables that were not normally distributed were analyzed using non-parametric tests. For quantitative variables, an independent t-test was used for normally distributed data, while Mann–Whitney U and Kruskal–Wallis tests were used for non-normally distributed data. Statistical significance was defined as $p<0.05$. The correlations between parameters were evaluated using Spearman's rank correlation analysis ($r\square$) because some variables did not follow a normal distribution. The strength of correlation coefficients was interpreted as weak (0.000–0.249), moderate (0.250–0.499), strong (0.500–0.749), and very strong (0.750–1.000).

RESULTS

Baseline demographic and clinical characteristics of the study population are presented in Table 2. The RAI-treated and RAI-untreated groups were comparable in terms of age and BMI, and no statistically significant differences were observed between the groups for these variables. The mean age of the RAI-treated group was 36.65 ± 6.68 years, whereas the mean age of the RAI-untreated group was 35.10 ± 7.96 years ($p = 0.557$). Similarly, BMI values were comparable between the two groups (28.2 ± 5.48 vs 26.7 ± 3.58 kg/m^2, $p = 0.339$). However, tumor diameter was significantly larger in the RAI-treated group compared with the RAI-untreated group (24.76 ± 13.8 mm vs 6.46 ± 3.59 mm, $p = 0.001$). In addition, TSH levels were significantly lower in the RAI-treated group (0.46 ± 0.43 µIU/mL vs 1.22 ± 0.91 µIU/mL, $p = 0.011$).

Biochemical parameters of the study groups are summarized in Table 3. AMH levels were significantly lower

Table 2. Demographic Characteristics

	RAI-treated Mean ± SD	RAI-untreated Mean ± SD	p
Age	36,65±6,68	35,10±7,96	0,557
BMI	28,2±5,48	26,7±3,58	0,339
Number of children		3,30±2,25	0,972
Age at RAI	33,5±6,59	-	-
RAI dose	109,24±22,58	-	-
Tumor diameter	24,76±13,8	6,46±3,59	0,001
TSH	0,46±0,43	1,22±0,91	0,011

Table 3. Biochemical parameters in the RAI-treated and RAI-Untreated groups

	RAI-treated Mean ± SD	RAI-untreated Mean ± SD	p
AMH	1,34±0,37	1,79±0,25	0,001
FSH	6,65±3,94	4,75±2,22	0,077
LH	4,95±3,51	4,48±2,68	0,603
E2	71,9±59,6	62,8±58,2	0,587

Table 4. Comparison of AMH levels according to RAI dose

	75 mci (n=3)	100 mci (n=33)	150 mci (n=10)	p
AMH	1,32±0,42	1,29±0,31	1,67±0,55	0,073

Table 5. Correlation between AMH and biochemical and demographic parameters

	RAI -treated (n=46)		RAI-untreatred (n=20)	
	rS	p	rS	p
Age	-0,181	0,265	0,081	0,764
Time since treatment	0,00	1,00	0,00	1,00
BMİ	-0,191	0,238	0,559	0,025
RAİ dose	0,116	0,475	-	-
TSH	-0,115	0,498	0,293	0,290
FSH	0,147	0,399	-0,543	0,045
LH	0,051	0,767	-0,345	0,208
E2	0,068	0,681	-0,233	0,422

in the RAI-treated group compared with the RAI-untreated group (1.34 ± 0.37 ng/mL vs 1.79 ± 0.25 ng/mL, p = 0.001). No statistically significant differences were observed between the two groups with respect to serum FSH, LH, or estradiol levels. When AMH levels were grouped according to RAI doses of 75, 100, and 150 mCi, no statistically significant differences was observed between RAI dose and AMH levels (p = 0.073) (Table 4). Spearman correlation analysis was performed to evaluate relationships between AMH levels and clinical parameters. In the RAI-untreated group, a strong negative correlation was observed between FSH and AMH levels (r□ = –0.543, p = 0.045) (Figure 3). In contrast, no significant correlations were detected between AMH levels and age, BMI, TSH, or RAI dose in the RAI-treated group (r□ = 0.559, p = 0.025) (Table 5).

To further evaluate the independent association between RAI therapy and AMH levels, a mul-tivariable linear regression analysis was performed, adjusting for potential confounders inclu-ding age, BMI, TSH level, tumor diameter, and time since treatment. As shown in Table 6, RAI therapy remained independently associated with lower AMH levels (β = –0.41, p = 0.003). Age was also significantly associated with AMH levels (β = –0.36, p = 0.010). In contrast, BMI, TSH level, tumor diameter, and time since treatment were not significant pre-dictors of AMH levels in the adjusted model. Menstrual irregularities were more frequently reported in the RAI-treated group. Among the 46 patients undergoing RAI therapy, only 8 (17.9%) reported a regular menstrual cycle, whereas 9 (45%) in the RAI-untreated group reported regular menstruation.

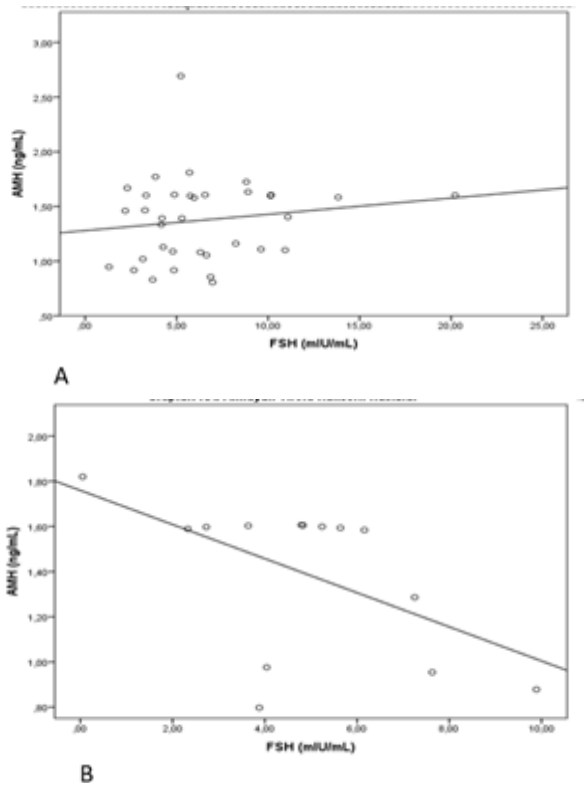

Figure 3. Correlation between AMH and FSH. A. RAI-treated (n=46, rs 0.147, p=0.238) and B. RAI-untreated (n=20, rs-0.543, p=0.045)

Table 6. Adjusted Multivariable Linear Regression Analysis for Factors Associated with AMH Levels

Variable	β (Standar-dized)	B (Unstandar-dized)	Standard Error	95% CI	p
RAI therapy (yes vs no)	−0.41	−0.45	0.14	−0.73 – −0.17	0.003
Age (years)	−0.36	−0.04	0.02	−0.07 – −0.01	0.010
BMI (kg/m^2)	−0.12	−0.02	0.02	−0.05 – 0.01	0.220
TSH (μIU/mL)	−0.08	−0.03	0.03	−0.08 – 0.02	0.310
Tumor diameter (mm)	−0.05	−0.01	0.01	−0.03 – 0.01	0.420
Time since treatment (months)	0.03	0.01	0.01	−0.01 – 0.03	0.560

DISCUSSION

The present study investigated the association between radioactive iodine (RAI) ablation therapy and ovarian reserve in premenopausal women with differentiated thyroid cancer. Our findings demonstrated that AMH levels were significantly lower in patients who received RAI therapy compared with those who did not receive RAI treatment. Since AMH is considered one of the most reliable biomarkers of ovarian reserve, these findings suggest that RAI therapy might be associated with reduced ovarian reserve in this patient population. According to the most recent American Thyroid Association (ATA) guidelines published in 2025, RAI therapy remains an important therapeutic option for selected patients with differentiated thyroid cancer, particularly in those with intermediate- and high-risk disease. However, the potential adverse effects of RAI therapy on reproductive function and gonadal tissues remain an important clinical concern, especially in young women of reproductive age (5).

Ovarian reserve represents the quantity and quality of the remaining follicular pool in the ovaries. Several serum markers have been used to evaluate reproductive status and ovarian reserve. Ovarian aging has been studied using AMH, FSH, LH, and estradiol levels. AMH is mainly secreted from primary and preantral follicles, and its levels are independent of those of gonadotropins. Low AMH levels are associated with natural ovarian aging and infertility (6). In addition, fluctuations in AMH levels during the menstrual cycle suggest that AMH plays a role in folliculogenesis (7). Since 1949, studies have reported the occurrence of early menopause following high-dose RAI therapy (8). Ceccarelli et al. reported an earlier age at menopause in women treated for thyroid cancer with RAI therapy and levothyroxine suppressive therapy compared with women treated with levothyroxine for goiter (9). In another study conducted in France in 1989, temporary amenorrhea lasting up to 12 months was documented in 27% of premenopausal women with thyroid cancer following RAI therapy (10). Women who developed temporary amenorrhea were older (38.9 ± 7.1 vs. 32.2 ± 6.1 years; p <0.001) and showed increased FSH levels. However, unlike in men and consistent with the authors' own observations, this effect was not related to the administered dose. These findings are consistent with the results of our study. In a study by Sawka et al., temporary amenorrhea observed in women receiving RAI ablation therapy after thyroid cancer was considered an acute effect of RAI treatment. The rate of temporary amenorrhea was reported to range between 12% and 30% among women who previously had regular menstrual cycles. The damage caused by RAI ablation therapy may contribute to the expected decline in ovarian function and may accelerate follicular atresia in premenopausal women by reducing the viable follicle pool. It has been estimated that ovarian damage after RAI therapy may cause menopause to occur approximately one year earlier than in the general population (11). However, based on analyses of retrospective studies conducted between 1960 and 2002 (12-15), it has been suggested that temporary menstrual irregularities are probably insignificant, as there is no clear evidence of reduced fertility in these women.

In our study, AMH levels were 1.34 ± 0.37 ng/mL in the group of patients with differentiated thyroid cancer who received RAI ablation therapy, while it was significantly higher in the control group at 1.79 ± 0.25 ng/mL (p = 0.001). Similarly, in a study conducted by Acıbucu et al. in 2016, AMH, FSH, LH, E2, TSH, and creatinine levels were compared between 45 premenopausal women with differentiated thyroid cancer treated with RAI and 40 healthy women; AMH levels were found to be lower in the RAI-treated group (16). In contrast to the healthy women included in the control group of the study by Acıbucu et al., the control group in our study consisted of women diagnosed with differentiated thyroid cancer.

Yaish et al., included 30 women with differentiated thyroid cancer who received RAI therapy. Baseline AMH measurements were obtained at 3, 6, 9, and 12 months according to RAI dose. None of the patients had previously received RAI or been exposed to radiation. The participants were aged 20-45 years. A significant decline in AMH levels were observed at all time points. Specifically, three months after RAI, AMH levels were 49% lower than baseline (1.9 ± 0.38 vs. 3.250 ± 0.56 ng/mL; p = 0.001). Partial recovery was subsequently observed, and AMH levels plateaued at nine months; however, concentrations at one year remained 32% below baseline (p = 0.016). AMH levels at 6, 9, and 12 months after treatment were 2.23 ± 0.43, 2.47 ± 0.47, and 2.36 ± 0.47 ng/mL, respectively. In 82% of the participants, final AMH levels remained below baseline values, indicating that serum AMH levels were still 32% lower one year after treatment (2.36 ± 1.88 ng/mL; p<0.005). The only continuous variables associated with AMH decline at three months were age (r = 0.51; p = 0.02) and age at menarche (r = 0.48; p = 0.03). Notably, RAI dose was not associated with AMH decline. None of the patients smoked or used oral contraceptives. Older patients (≥35 years) were significantly more likely to experience a marked decrease in AMH at three months compared with younger patients (63.7% ± 18.5 vs

33.1% ± 29.2; p = 0.01) (17). Consistent with our study, ovarian reserve was adversely affected in women with differentiated thyroid cancer receiving RAI ablation therapy, and RAI dose did not have a significant effect on AMH levels (p = 0.073).

Supporting our findings, Evranos et al. conducted a study in Turkey in 2018 that included 33 premenopausal women with differentiated thyroid cancer who received RAI ablation therapy. AMH, FSH, LH, and E2 levels were measured during the follicular phase at 3, 6, and 12 months after RAI therapy. The mean AMH level prior to RAI ablation therapy was 3.25 (0.32–17.42) ng/mL, while AMH levels at 3, 6, and 12 months after treatment were 1.00 (0.01–3.93), 1.13 (0.08–6.12), and 1.37 (0.09–6.1) ng/mL, respectively. The authors observed a significant decrease in AMH levels following RAI ablation therapy (p = 0.001) (18). In our study, consistent with the findings of Evranos et al., no significant differences were observed in FSH, LH, and E2 levels after RAI therapy (p > 0.05). FSH levels fluctuate during the menstrual cycle; therefore, repeated measurements are required. AMH levels, however, are more stable. FSH, E2, and inhibin B indirectly reflect ovarian reserve, but cyclic variation complicates their correlation with ovarian reserve. As observed in our study and previous studies, while variability was noted in FSH and E2 levels when assessing ovarian reserve, AMH levels were relatively more stable. Measurement of AMH levels is recommended for evaluating age-related gonadal reserve in premenopausal women with thyroid cancer (19).

In our study of premenopausal women with a history of differentiated thyroid cancer, AMH levels were significantly lower (1.34 ± 0.37 ng/mL; p = 0.001) in the group receiving ablative RAI therapy following thyroidectomy. In contrast, Giusti et al. reported no significant differences in AMH levels between 34 women treated with RAI and 23 women who did not receive RAI among 57 patients with differentiated thyroid cancer (20). In the study by Giusti et al., the mean age was 40.7 ± 6.7 years in the RAI-treated group and 41.6 ± 7.4 years in the control group, whereas in our study, the mean age was 36.65 ± 6.68 years in the RAI-treated group and 35.10 ± 7.96 years in the control group. This difference in age distribution may account for the discrepancies between the findings. Indeed, in a study conducted by Lee et al. in healthy women, the mean AMH level was 2.3 ng/mL in women aged 38–40 years and 1.4 ng/mL in women aged 40–43 years (21). In addition, AMH shows small inter and intra-cycle variability and gradually declines with age, and AMH levels become undetectable after menopause (22,23).

More recent studies have also evaluated ovarian reserve and reproductive outcomes in women undergoing RAI therapy. Kim et al. reported that radioactive iodine therapy may be associated with a measurable decline in ovarian reserve markers, particularly AMH levels, in women with differentiated thyroid cancer (24). Similarly, Anderson et al. emphasized that cancer therapies involving ionizing radiation may adversely affect ovarian reserve and reproductive function in young female patients (25). In addition to hormonal markers, recent studies have also investigated long-term reproductive outcomes in thyroid cancer survivors. Lamartina et al. reported that although ovarian reserve markers may decline following treatment, many thyroid cancer survivors maintain the ability to conceive and achieve successful pregnancies (26). Likewise, Rizzo et al. demonstrated that fertility and pregnancy outcomes after RAI therapy are generally reassuring, although careful reproductive counseling may be warranted for women of reproductive age undergoing treatment (27). Unfortunately, long-term fertility outcomes, such as pregnancy rates, or live birth rates were not systematically recorded in our cohort. Future studies assessing reproductive outcomes after RAI therapy would provide more clinically meaningful insights.

Study Limitations

This study has several limitations. First, its retrospective and single-center design may limit the generalizability of the findings and introduce potential selection bias. Second, baseline pre-treatment AMH levels were not available, which precluded an intra-individual longitudinal assessment of ovarian function before and after radioactive iodine therapy. Third, the relatively small sample size, particularly in the RAI-untreated control group, may reduce the statistical power to detect subtle associations, including dose–response relationships. In addition, other important determinants of ovarian reserve such as smoking status, detailed reproductive history, and long-term fertility outcomes were not systematically captured. Another important limitation is the relatively small sample size and single-center design of the study. These factors may limit the generalizability of the findings and reduce statistical power. Therefore, multicenter studies with larger patient populations are required to validate these observations. Finally, hormonal measurements were obtained at a single time point, and dynamic changes over time could not be evaluated in this study. Therefore, larger prospective studies with longitudinal hormonal and reproductive outcome assessments are required to confirm and extend our findings.

CONCLUSION

In conclusion, our findings demonstrate an association between RAI therapy and lower AMH levels in premenopausal women with differentiated thyroid cancer. These findings suggest that RAI therapy may be associated with reduced ovarian reserve. However, due to the cross-sectional design and the absence of baseline AMH measurements, causal inference cannot be established. Larger prospective studies are needed to further clarify this relationship.

DECLARATIONS

Conflict of Interest: *The authors declare no conflicts of interest related to this study.*

Financial Disclosure: *The authors declare no financial conflict of interest related to this study.*

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