Hindawi Publishing Corporation
Advances in Endocrinology
Volume 2015, Article ID 436768, 5 pages
http://dx.doi.org/10.1155/2015/436768

Clinical Study

Mean Platelet Volume in Hyperthyroid Toxic Adenoma Patients after Radioactive ^{131}I Treatment

Eda Simsek,[1] Ozge Timur,[2] Ayse Carlioglu,[3] Senay Arikan Durmaz,[3] Munir Demirci,[4] and Hakan Sevimli[2]

[1]*Erzurum Regional Training and Research Hospital, Department of Otorhinolaryngology, 251000 Erzurum, Turkey*
[2]*Erzurum Regional Training and Research Hospital, Department of Internal Medicine, 251000 Erzurum, Turkey*
[3]*Erzurum Regional Training and Research Hospital, Department of Endocrinology, 251000 Erzurum, Turkey*
[4]*Erzurum Regional Training and Research Hospital, Department of Nuclear Medicine, 251000 Erzurum, Turkey*

Correspondence should be addressed to Ozge Timur; ozgetimur@yahoo.com

Received 22 August 2015; Accepted 28 October 2015

Academic Editor: Zahra Fatehi-Hassanabad

This study demonstrates that mean platelet volume (MPV) levels decrease after radioiodine (RAI) ablation therapy in hyperthyroid patients. Regarding the fact that large platelets are hemostatically more active, we suggest that hyperthyroid patients are at risk of cardiovascular disease despite all other cardiovascular risk factors. After RAI ablation therapy as MPV levels return to normal, cardiovascular risk for hyperthyroid patients reduces.

1. Introduction

Since 1940s, radioactive ^{131}I (RAI) therapy has been a major component of the treatment of hyperthyroidism and differentiated thyroid cancer. RAI is the most common definitive treatment of hyperthyroidism [1]. There are no definitive data that provide evidence for increased rates of thyroid cancer, leukaemia, infertility, or neonatal abnormality in patients treated with radioiodine. Radioiodine therapy is safe, definitive, and cost-effective [2].

Mean platelet volume (MPV) is the measure of platelet size. MPV possibly is a simple way to estimate platelet activity [3]. Activated platelets play an important role in the pathogenesis of vascular disease especially coronary heart diseases. Larger platelets are metabolically and enzymatically more active and have greater prothrombotic potential. Elevated MPV is associated with other markers of platelet activity, including increased platelet aggregation, increased thromboxane synthesis, and increased expression of adhesion molecules [4–6]. Increased platelet size has been observed to be associated with known cardiovascular risk factors such as smoking, diabetes mellitus, obesity, and hypertension [7–10].

Previous reports suggested that hyperthyroidism and hypothyroidism were associated with increased risks for thrombosis and bleeding. Recently, a lot of studies associated with high mean platelet level (MPV) in patients with hypo- and hyperthyroidism have been reported in medical literature. Panzer et al. studied platelets in hyperthyroidism and found out that MPV increases in hyperthyroidism [11]. But it is not clear whether or not radioactive iodine treatment has effect on platelet activity.

Aim of our preliminary study is to determine the platelet size via MPV level in hyperthyroid toxic adenoma patients undergoing radioactive iodine ablation treatment.

2. Materials and Methods

Thirty-four toxic adenoma patients with hyperthyroidism treated with a therapeutic dose of ^{131}I in our Endocrinology Clinic at Erzurum Region Training and Research Hospital between 2009 and 2013 were included this study. The control group includes 34 age, sex, and body mass index matched healthy subjects. Ethics Committee of Erzurum Region Training and Research Hospital approved the study design. All the study subjects provided written informed consent.

Patients treated with radioiodine received a single therapeutic dose of ^{131}I (range 8–15 μCi). FT_3, FT_4, and TSH levels

were performed before and after the RAI ablation treatment. All these parameters were reevaluated at least after eight months from RAI ablation treatment.

None of the patients were receiving antithyroid drugs. Patients were not given any drugs affecting platelet function at least for 2 weeks (e.g., acetylsalicylate, antiepileptics, heparin, and antithyroid drugs). Chronic illness, smoking, and having alcohol were also exclusion criteria.

2.1. Laboratory Assessment. In order to eliminate the conditions that can affect MPV levels and can cause tendency to cardiovascular diseases, fasting glucose and serum lipids were evaluated. Subjects taking medications which can affect platelet size or/and function are also eliminated. Blood glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) were measured by standard laboratory methods on a biochemistry autoanalyzer (Beckman Coulter AU 2700 Plus clinical chemistry autoanalyzer) with the company's original kits.

Thyroid hormones were determined by Abbott Architect i2000 chemiluminescence microparticle immunoassay (CMIA).

MPV was measured in a blood sample collected in EDTA. The Beckman Coulter LH 750 (impedance method) analyzers were used for complete blood counts. All hormonal analyses were performed by chemiluminescence assay.

Body mass index was calculated by the ratio between weight and height squared in kg/m^2.

2.2. Statistical Analysis. Data are presented as mean ± SD. The IBM SPSS Statistics version 17 was used for statistical analysis. Student's t-test was done to find the significance of difference between means whenever applicable. One-tailed Pearson's correlation test was done to find the correlation between various variables. Linear regression analysis was done whenever appropriate. Chi square test, Chi square with Yates correction, and Fisher's exact test, wherever applicable, were done to test the association between two findings.

3. Results

Clinical and demographic characteristics of the groups are shown in Table 1. There were no significant differences in age (42.12 ± 8.42, 37.33 ± 8.62 years, resp., $p > 0.005$), sex, body mass index (25.83±2.72, 24.49±2.59 kg/m^2, resp., $p > 0.005$), and waist circumference (91.00 ± 9.04, 85.27 ± 10.35, resp., $p > 0.005$) between study and control groups.

Laboratory parameters are shown in Table 2. The mean FT_3 levels were 4.5 ± 1.6 pg/mL; the mean FT_4 levels were 1.4 ± 0.6 pg/dL; the mean TSH levels were 0.06 ± 0.08 μIU/mL before RAI treatment. After RAI treatment, the mean FT_3 levels were 3.07 ± 0.5 pg/mL; the mean FT_4 levels were 1.1 ± 0.2 pg/dL; the mean TSH levels were 1.6 ± 1.3 μIU/mL. Serum FT_3 levels were significantly higher (4.54 ± 1.67 and 3.14 ± 0.79 pg/dL, resp., $p = 0.00$) and serum TSH levels were significantly lower (0.27 ± 0.69 and 1.59 ± 0.27 μIU/mL, resp., $p = 0.00$) in study group before RAI treatment.

Table 1: The clinical characteristics of the study group.

	RAI treatment group	Control group
N	34	34
Age (yr)	42.12 ± 8.42	37.33 ± 8.62
Gender (M/F)		
BMI (kg/m^2)	25.83 ± 2.72	24.49 ± 2.59
Waist circumference	91.00 ± 9.04	85.27 ± 10.35

Table 2: The clinical and biochemical features of RAI treatment and controls.

	RAI treatment group	Control group
N	34	34
MPV (fL)	8.53 ± 1.28	7.92 ± 0.91
Platelet count ($\times 10^3/\mu$L)	265285 ± 68695	254411 ± 58584
Triglyceride (mg/dL)	162.67 ± 109.17	98.05 ± 43.11
Total cholesterol (mg/dL)	184.87 ± 35.82	199.87 ± 46.70
HDL-C (mg/dL)	48.00 ± 11.50	58.17 ± 18.13
LDL-C (mg/dL)	110.96 ± 39.73	132.16 ± 38.01
FT_3 (pg/mL)	4.54 ± 1.67*	3.14 ± 0.79*
FT_4 (pg/mL)	1.42 ± 0.66	1.53 ± 0.87
TSH (μIU/mL)	0.27 ± 0.69*	1.59 ± 1.05*
CRP (mg/dL)	2.69 ± 5.36	1.88 ± 1.39

HDL: high-density lipoprotein; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone.
* $p < 0.05$ for RAI patients compared with controls.

Table 3: The clinical and biochemical features of patients before and after RAI treatment.

	Before RAI treatment	After RAI treatment
Triglyceride (mg/dL)	162.67 ± 109.17	154.08 ± 77.34
Total cholesterol (mg/dL)	184.87 ± 35.82	187.48 ± 34.90
HDL-C (mg/dL)	48.00 ± 11.50	46.80 ± 10.96
LDL-C (mg/dL)	110.96 ± 39.73	122.60 ± 31.76
FT_3 (pg/mL)	4.54 ± 1.67	3.03 ± 0.54
FT_4 (pg/mL)	1.42 ± 0.66	1.12 ± 0.28
TSH (μIU/mL)	0.27 ± 0.69	1.88 ± 1.54

HDL: high-density lipoprotein; LDL: low-density lipoprotein; TSH: thyroid stimulating hormone.

There was no significant difference in serum FT_4 levels between groups. Serum triglyceride levels, total cholesterol, fasting glucose, and low-density lipoprotein (LDL) levels were similar between two groups. Patients characteristics before and after RAI treatment are shown in Table 3.

The mean platelet volume (MPV) levels before RAI treatment were significantly higher than MPV levels after RAI treatment (8.5 ± 1.2 and 8.0 ± 1.2 fL, resp., $p = 0.00$) (Figure 1).

Table 4: Multiple regression analysis of clinical factors possibly affecting the MPV in toxic adenoma subjects adjusted forage.

	β	p value
Age	−0.15	0.70
Gender	0.37	0.22
TSH	−0.85	0.04
FT_3	0.53	0.17
FT_4	0.60	0.12
BMI	0.11	0.76
Total cholesterol	−0.79	0.03

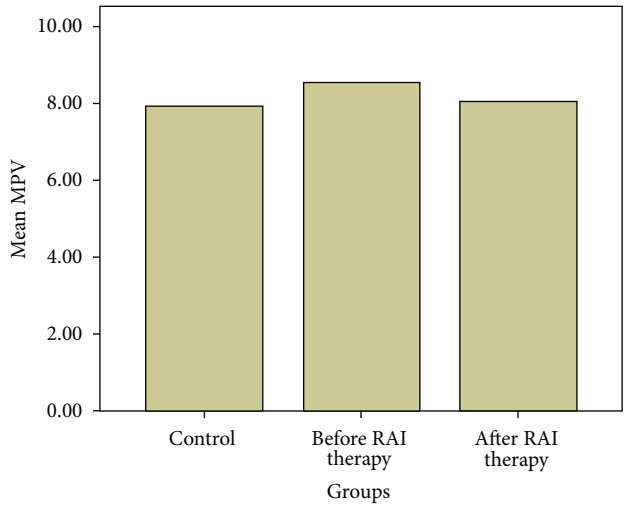

Figure 1: Mean MPV levels before and after RAI treatment and control group.

Multiple regression analysis with MPV as dependent variable and age, gender, BMI, total cholesterol, TSH, FT_3, and FT_4 as independent variables was performed. TSH and total cholesterol levels were predictive variables for MPV (Table 4).

4. Discussion

This study demonstrates that MPV levels decrease after RAI ablation therapy in hyperthyroid patients. Regarding the fact that large platelets are hemostatically more active, we suggest that hyperthyroid patients are at risk of cardiovascular disease despite all other cardiovascular risk factors. After RAI ablation therapy, as MPV levels return to be normal, cardiovascular risk for hyperthyroid patients reduces.

RAI ablation therapy is indicated in patients with nearly all causes of hyperthyroidism and is considered the treatment of choice for most patients with Graves' hyperthyroidism who are beyond the adolescent years. There are no definitive data that provide evidence for increased rates of thyroid cancer, leukaemia, infertility, or neonatal abnormality in patients treated with radioiodine. Radioiodine therapy is safe, definitive, and cost-effective [1]. In our study all of the patients were toxic adenoma patients. Tarantini et al. evaluated the outcome of 100 patients with hyperthyroidism (Graves' disease, toxic adenoma, and toxic multinodular goiter). They found out that after 3 years %75 of toxic adenoma patients were euthyroid who were treated with RAI. Their results indicate that RAI therapy is highly effective and safe for the control of hyperthyroidism [2]. Also Erem et al. showed that a single fixed dose of 10 μCi of RAI is highly effective in curing GD as well as toxic nodular hyperthyroidism [12].

Since platelets play a crucial role in the pathogenesis of thrombotic diseases, it had been proposed that increased MPV might be a cardiovascular risk factor [4, 5]. Larger platelets contain more granules and produce greater amounts of vasoactive and prothrombotic factors, such as thromboxane A2, serotonin, and ATP; they aggregate more rapidly. Thromboxane A2 causes vasoconstriction and vein occlusion. Increased MPV values are reported in various cardiovascular diseases [13–15]. Endler et al. reported that, regardless of the extent of the coronary lesions among patients with coronary artery disease, those with higher MPV values had been found to have a greater risk of acute myocardial infarction than those with lower MPV [14]. Pizzulli et al. reported higher MPV values in patients with documented coronary artery disease than that in controls [15].

Thyroid hormones are essential for human metabolism, growth, and normal development. All cells are targets for thyroid hormones. To our knowledge thyroid hormones have numbers of action on platelet functions. Both thyroid dysfunction and autoimmune thyroid diseases can cause thrombosis or hemorrhage affecting primary or secondary hemostasis [16, 17]. It has been observed that thrombocytopenia is associated with hyperthyroidism and an immune mediated mechanism could play role [18–20]. But on the other hand an increase in megakaryocytes and decrease in platelet survival time are observed in hyperthyroid patients even if platelet count is normal [21, 22]. In our study all of our patients were toxic adenoma patients. Toxic adenoma is a nonautoimmune disease and all the thyroid antibodies were negative. In previous studies autoimmune mechanisms for MPV levels were evaluated. But in our study we evaluated nonautoimmune thyroid disease and MPV levels. So we can claim that MPV levels are associated with TSH levels but not with autoimmune mechanisms. As the TSH levels became normal with RAI treatment, MPV levels decreased.

Alcelik et al. showed platelet function in euthyroid patients undergoing thyroidectomy [23]. They showed that thyroidectomy does not affect platelet activation in euthyroid patients and the association between thyroid diseases and MPV levels is depending on thyroid hormone status. In our study, MPV levels decreased independent from TSH in univariate and multivariate linear regression analysis. We suggest that this finding is related to RAI therapy.

Panzer et al. compared in 15 patients with hyperthyroidism (11 with Graves' disease, 3 with toxic adenoma, and 1 with multinodular goiter) platelet counts and MPV before and 3 weeks after initiation of antithyroid drug therapy when the patients were euthyroid. They showed that after 3 weeks of antithyroid drug therapy there was a significant increase in platelet count and a decrease in MPV (10.6 fL

before treatment, 9.87 fL after treatment) compared with the pretreatment values [11]. Ford et al. evaluated 28 hyperthyroid patients and they found that MPV levels were higher in hyperthyroid state and, on return to the euthyroid state, there were highly significant falls in the mean platelet volume [24]. In contrast to Panzer et al.'s study, Ford et al. did not find significant change in mean platelet count when comparing their pre- and posttreatment data. This might be explained with the reexamination time as Ford et al. reexamined patients after 4-week period of antithyroid treatment where Panzer et al. did that after 3 weeks. It is conceivable that platelet count rises initially when euthyroidism is induced in hyperthyroid patients and decreases when euthyroidism is maintained. As we reevaluated patients after eight months and all the patients were still in euthyroid state, we did not find any changes in platelet count. Our pretreatment MPV levels decreased after RAI treatment (8.5 ± 1.2 and 8.0 ± 1.2 fL, resp., $p = 0.00$).

Okada et al. showed that platelet epidermal growth factor (EGF) was increased in patients with untreated Graves' disease compared with the healthy control. After treatment of hyperthyroidism the EGF concentration in platelets significantly decreased [25]. Shortened platelet survival has been observed in many studies of patients with hyperthyroidism and is thought to be due to enhanced splenic sequestration [26, 27]. Accordingly, patients with hyperthyroidism would have greater numbers of younger platelets which contain more EGF. In support of this, it is known that the size of platelets decreases with their age, and the MPV in the patients with hyperthyroidism is larger than in euthyroid patients or normal controls [25].

We have shown that MPV was independently associated with total cholesterol level. In their study, Icli et al. have shown that MPV was increased in patients with familial hypercholesterolemia and that it was independently associated with total cholesterol level [28]. As is known, increased total cholesterol levels increase the risk of cardiovascular diseases.

Higher MPV levels are associated with hyperthyroidism. Previous studies show that MPV levels return to normal after patients were euthyroid with antithyroid drug therapy [11]. This study indicates that MPV levels return to normal after RAI ablation therapy. There was no significant difference between pre- and posttreatment hematocrit, red blood cell counts, and mean red blood volumes; therefore, the decrease in MPV could not be explained by changes in osmolality or plasma volume reduction. This is the first study reporting that RAI ablation therapy is effective in reducing MPV levels in hyperthyroid patients. As MPV levels return to normal, cardiovascular risks of hyperthyroid patients related to high MPV levels reduce.

Thus, in hyperthyroid toxic adenoma patients, radioiodine therapy can be protecting from the cardiovascular risks. Further studies are needed to understand the relationship between radioiodine therapy and MPV levels in hyperthyroid patients to prevent from cardiovascular risks.

Conflict of Interests

The authors declare no conflict of interests.

References

[1] S. L. Lee, "Radioactive iodine therapy," *Current Opinion in Endocrinology, Diabetes and Obesity*, vol. 19, no. 5, pp. 420–428, 2012.

[2] B. Tarantini, C. Ciuoli, G. Di Cairano et al., "Effectiveness of radioiodine (131-I) as definitive therapy in patients with autoimmune and non-autoimmune hyperthyroidism," *Journal of Endocrinological Investigation*, vol. 29, no. 7, pp. 594–598, 2006.

[3] S. Greisenegger, G. Endler, K. Hsieh, S. Tentschert, C. Mannhalter, and W. Lalouschek, "Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events?" *Stroke*, vol. 35, no. 7, pp. 1688–1691, 2004.

[4] A. Y. Gasparyan, L. Ayvazyan, D. P. Mikhailidis, and G. D. Kitas, "Mean platelet volume: a link between thrombosis and inflammation?" *Current Pharmaceutical Design*, vol. 17, no. 1, pp. 47–58, 2011.

[5] S. G. Chu, R. C. Becker, P. B. Berger et al., "Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis," *Journal of Thrombosis and Haemostasis*, vol. 8, no. 1, pp. 148–156, 2010.

[6] E. Coban, G. Yazicioglu, and M. Ozdogan, "Platelet activation in subjects with subclinical hypothyroidism," *Medical Science Monitor*, vol. 13, no. 4, pp. 211–214, 2007.

[7] S. Nadar, A. D. Blann, and G. Y. H. Lip, "Platelet morphology and plasma indices of platelet activation in essential hypertension: effects of amlodipine-based antihypertensive therapy," *Annals of Medicine*, vol. 36, no. 7, pp. 552–557, 2004.

[8] R. Pathansali, N. Smith, and P. Bath, "Altered megakaryocyte-platelet haemostatic axis in hypercholesterolaemia," *Platelets*, vol. 12, no. 5, pp. 292–297, 2001.

[9] K. Kario, T. Matsuo, and K. Nakao, "Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis," *Clinical and Laboratory Haematology*, vol. 14, no. 4, pp. 281–287, 1992.

[10] E. Coban, M. Ozdogan, G. Yazicioglu, and F. Akcit, "The mean platelet volume in patients with obesity," *International Journal of Clinical Practice*, vol. 59, no. 8, pp. 981–982, 2005.

[11] S. Panzer, A. Haubenstock, and E. Minar, "Platelets in hyperthyiroidism: studies on platelet counts, mean platelet volume, 111-indium-labeled platelet kinetics, and platelet-associated immunoglobulins G and M," *The Journal of Clinical Endocrinology & Metabolism*, vol. 70, no. 2, pp. 491–496, 1990.

[12] C. Erem, N. Kandemir, A. Hacihasanoglu, H. Ö. Ersöz, K. Ukinc, and M. Kocak, "Radioiodine treatment of hyperthyroidism: prognostic factors affecting outcome," *Endocrine*, vol. 25, no. 1, pp. 55–60, 2004.

[13] L. Vizioli, S. Muscari, and A. Muscari, "The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases," *International Journal of Clinical Practice*, vol. 63, no. 10, pp. 1509–1515, 2009.

[14] G. Endler, A. Klimesch, H. Sunder-Plassmann et al., "Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease," *British Journal of Haematology*, vol. 117, no. 2, pp. 399–404, 2002.

[15] L. Pizzulli, A. Yang, J. F. Martin, and B. Lüderitz, "Changes in platelet size and count in unstable angina compared to stable angina or non-cardiac chest pain," *European Heart Journal*, vol. 19, no. 1, pp. 80–84, 1998.

[16] J. J. Van Doormaal, J. van der Meer, H. R. Oosten, M. R. Halie, and H. Doorenbos, "Hypothyroidism leads to more small-sized platelets in circulation," *Thrombosis and Haemostasis*, vol. 58, no. 4, pp. 964–965, 1987.

[17] H. C. Ford and J. M. Carter, "Moderate, chronic hypothyroidism does not lead to more small-sized platelets in the circulation," *Thrombosis and Haemostasis*, vol. 60, no. 3, p. 524, 1988.

[18] J. S. Marshall, A. S. Weisberger, R. P. Levy, and R. T. Breckenridge, "Coexistent idiopathic thrombocytopenic purpura and hyperthyroidism," *Annals of Internal Medicine*, vol. 67, no. 2, pp. 411–414, 1967.

[19] K. Hymes, M. Blum, H. Lackner, and S. Karpatkin, "Easy bruising, thrombocytopenia, and elevated platelet immunoglobulin G in Graves' disease and Hashimoto's thyroiditis," *Annals of Internal Medicine*, vol. 94, no. 1, pp. 27–30, 1981.

[20] A. R. Axelrod and L. Berman, "The bone marrow in hyperthyroidism and hypothyroidism," *Blood*, vol. 6, no. 5, pp. 436–453, 1951.

[21] B. A. Lamberg, V. Kivikangas, R. Pelkonen, and P. Vuopio, "Thrombocytopenia and decreased life-span of thrombocytes in hyperthyroidism," *Annals of Clinical Research*, vol. 3, no. 2, pp. 98–102, 1971.

[22] Y. Kurata, Y. Nishioeda, T. Tsubakio, and T. Kitani, "Thrombocytopenia in Graves' disease: effect of T3 on platelet kinetics," *Acta Haematologica*, vol. 63, no. 4, pp. 185–190, 1980.

[23] A. Alcelik, G. Aktas, M. Eroglu et al., "Platelet function in euthyroid patients undergoing thyroidectomy in women," *European Review for Medical and Pharmacological Sciences*, vol. 17, no. 17, pp. 2350–2353, 2013.

[24] H. C. Ford, R. J. Toomath, J. M. Carter, J. W. Delahunt, and J. N. Fagerstrom, "Mean platelet volume is increased in hyperthyroidism," *American Journal of Hematology*, vol. 27, no. 3, pp. 190–193, 1988.

[25] M. Okada, Y. Kamiya, J. Ito et al., "Platelet epidermal growth factor in thyroid disorders," *Endocrine Journal*, vol. 45, no. 1, pp. 83–88, 1998.

[26] V. Fuster, J. H. Chesebro, R. L. Frye, and L. R. Elveback, "Platelet survival and the development of coronary artery disease in the young adult: effects of cigarette smoking, strong family history and medical therapy," *Circulation*, vol. 63, no. 3, pp. 546–551, 1981.

[27] C. W. Baldrlge and F. R. Peterson, "Splenic enlargement in hyperthyroidism," *Journal of the American Medical Association*, vol. 88, pp. 1701–1702, 1927.

[28] A. Icli, F. Aksoy, G. Nar et al., "Increased mean platelet volume in familial hypercholesterolemia," *Angiology*, 2015.