
Association between tumor stage and grade and mean platelet volume in patients with renal cell carcinoma

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Abstract: Purpose: To research association between Mean Platelet Volume (MPV) and tumor stage and grade in non-metastatic renal cell carcinomas in circumstances of hypoxia, thromboembolism, and ischemia, based on MPV increase. Material and methods: Data of 104 non-metastatic patients, in whom nephrectomy was done and whose pathology resulted in renal cell carcinoma, have been evaluated retrospectively. The patients were clinically classified as T1a, T1b, T2a, T2b according to TNM stage and as Fuhrman Grade 1, 2, 3, 4 according to pathology results. Preoperative mean platelet number and MPV values of the patients were compared with their tumor stage and grade. Results: Sixteen (15%) were in T1a, 41 (39%) were in T1b, 39 (38%) were in T2a, and 8 (7%) of the patients were in T2b clinical stage. According to pathology results, 21 (20%) were assessed as Fuhrman grade I, 59 (57%) were grade II, 22 (21%) were grade III, and 2 (2%) of the patients were grade IV. Mean MPV values were 8.50 ± 1.39 , 8.51 ± 1.25 , 8.65 ± 1.12 , and 8.95 ± 0.07 in Grade I, II, III, IV, respectively. A positive correlation was present between mean MPV and grade ($r = 0.052$, $p = 0.599$). As long as grade increases, mean MPV values were observed to increase. However, no statistically difference was determined between tumor grade and mean MPV and platelet (p values: 0.935 and 0.963, respectively). No statistically significant difference was detected between tumor stage and mean MPV and platelet (p values: 0.996 and 0.397, respectively). Conclusion: A positive correlation was observed to be between mean MPV values and tumor grade. However, no statistically significant difference was determined. It can be supported with the larger series that MPV for renal tumors, that is rapidly and expansively growing tumor, can be an effective biochemical indicator in early diagnosis, staging, and evaluation of response to treatment.

Keywords: Renal Cell Carcinoma, Stage, Grade, Mean Platelet Volume

1. Introduction

The prevalence of renal cancers among urogenital cancers is at the 3rd rank after prostate and bladder cancers. Renal Cell Carcinoma (RCC) constitutes 90% of these tumors [1]. When diagnosed, metastasis is present approximately in 30% of the patients with renal cell cancer; these tumors are resistant to chemotherapy and radiotherapy; and the rate of response to hormonotherapy is low [2,3].

Although the most effective treatment method in patients with RCC limited to organ is surgery, the recurrence rate over 35% has been reported in a 5-year postoperative period [4,5]. Tumor stage is one of the most important prognostic factors affecting survey. Therefore, the early diagnosis of potentially resectable mass may enable improved patient survival. In the literature, although various tumor indicators to be used for diagnosis and clinical follow-up of renal cell carcinomas have been reported, today, a tumor indicator of which reliability is

high and which is specific to renal cell carcinoma has not been described yet [2,6].

Platelets (Thrombocyte) have a crucial role in pathophysiology of diseases prone to thrombosis and inflammation [7]. Platelet size has been shown to reflect platelet activity [8]. Greater platelets include greater granules, are enzymatically and metabolically more active, and have more prothrombotic activity [9].

Mean Platelet Volume (MPV) is a potential marker most frequently used to measure platelet size and indicating platelet reactivity [10]. Increased platelet activation involves in development of atherosclerosis [11]. MPV levels elevate in vascular instances such as ischemia, venous thromboembolism, arterial thrombosis, acute ischemic syndrome (myocardial ischemia, cerebrovascular infarct) [12,13,14]. Furthermore, Varol et al. has shown high MPV in chronic hypoxia patients with severe obstructive apnea syndrome [15].

In our study, we also aimed to research the association between MPV and stage and grade of non-metastatic renal cell carcinomas, based on MPV increase in cases of hypoxia, thromboembolism, and ischemia.

2. Material and Methods

Data of a total of 104 patients, in whom multi-centered radical nephrectomy or partial nephrectomy were performed due to diagnosis of renal mass and whose pathology resulted in renal cell carcinoma, have been evaluated retrospectively. Tumor dimension of all patients were measured investigating their preoperative computed tomography (CT); their clinical staging according to TNM classification and their pathologic grade according to Fuhrman grading system have been noted reviewing pathologic reports. The patients have been classified as T1A, T1B, T2A, and T2B according to TNM stage and as Fuhrman Grade I, II, III, IV according to pathology results. The patients who have a history of chronic obstructive lung disease, thromboembolism, obstructive sleep apnea, acute and/or chronic renal failure, liver function disorder or any inflammatory disease in their anamnesis have been excluded from the study.

PLT and MPV values of all patients have been noted examining their preoperative hemogram parameters. The normal reference range given for MPV values was 6-11 fL. The normal reference limit for PLT was 150-400 $10^3 \mu\text{L}$. Preoperative PLT and MPV values of the patients were compared with tumor stage and grade.

Statistical analyses were performed using SPSS version 16.0 Windows version 16.0 (SPSS Inc. Chicago, IL). Firstly, conformity of all parameters to the normal distribution was assessed with Kolmogorov-Smirnov test. In comparison of mean values of data, One-Way Anova test was applied. In correlation analysis, Pearson correlation test was used. When P is <0.05 , it was accepted statistically significant. Data were presented as means \pm standard deviation.

3. Results

The mean age of the patients was 61 ± 12 (36-86). Sixty

seven (64%) of 104 patients included into the study were male, 37 (36%) were female patients. Sixteen (15%) of the patients staged according to TNM classification were in T1a, 41 (39%) were in T1b, 39 (38%) were in T2a, and 8 (7%) were in T2b clinical stage. According to pathology results, 21 (20%) were Fuhrman grade I, 59 (57%) were grade II, 22 (21%) were grade III, and 2 (2%) of the patients were evaluated as grade IV. When pathologic sub-types were considered, 53 (51%) were clear cell carcinoma, 28 (27%) were sarcomatoid carcinoma, 14 (13%) were papillary carcinoma, 6 (6%) were cystic renal cell carcinoma and 3 (3%) were chromophobe cell carcinoma. The mean MPV values was the lowest in grade-I patients and found 8.50 ± 1.39 ; the mean MPV value in grade-IV patients was the highest and found 8.95 ± 0.07 (Table-1). A positive correlation was detected between grade and MPV ($r = 0.052$, $p = 0.599$) (Figure-1). As long as grade of disease increases, the mean MPV value was observed to increase.

However, statistically no significant difference was determined when grade and mean MPV and mean PLT values were compared (p values: 0.935 and 0.963, respectively) (Table-1). When clinical stage and mean MPV and mean PLT values were compared, statistically no significant difference was detected (p values: 0.996 and 0.397, respectively) (Table-1)

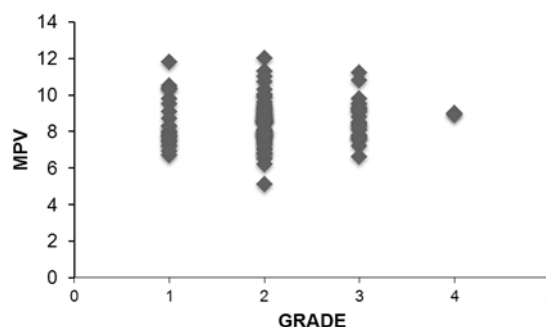


Figure 1. Correlation between Grade and MPV ($p = 0.599$, $r = 0.052$)
Abbreviation; MPV: Mean Platelet Volume

Table 1. Mean MPV and PLT values according to clinical stage and grade of disease. (Abbreviation; MPV: Mean Platelet Volume, PLT: Platelet)

| Stage-Grade | n (%) | MPV (fL) Mean \pm SD | P value ⁺ | PLT ($\times 10^3 \mu\text{L}$) Mean \pm SD | P value ⁺ |
|-------------|----------|---------------------------|-------------------------|--|-------------------------|
| T1a | 16 (15%) | 8.61 ± 0.88 | | 316.37 ± 108.70 | |
| T1b | 41 (39%) | 8.53 ± 1.13 | 0.996 | 296.9 ± 104.08 | 0.397 |
| T2a | 39 (38%) | 8.53 ± 1.46 | | 273.03 ± 96.04 | |
| T2b | 8 (7%) | 8.57 ± 1.32 | | 326.37 ± 154.91 | |
| Grade 1 | 21 (20%) | 8.50 ± 1.39 | | 282.95 ± 110.18 | |
| Grade 2 | 59 (57%) | 8.51 ± 1.25 | 0.935 | 295.28 ± 110.01 | 0.963 |
| Grade 3 | 22 (21%) | 8.65 ± 1.12 | | 298.36 ± 100.21 | |
| Grade 4 | 2 (2%) | 8.95 ± 0.07 | | 283.00 ± 63.65 | |

+ One-Way Anova test

4. Discussion

Renal cell carcinoma (RCC) is the most seen 3rd tumor among urogenital carcinomas and the most fatal one of urologic cancers. About 40% of RCC patients may be lost because of this disease; on the contrary, this rate in bladder and prostate cancers is approximately 20% [2,16].

To use nephron protective surgery more common in renal tumors day by day, increase of the rates of incidental detection, and early diagnosis have increased the need of tumor indicators in RCC even more [2]. In prediction of prognosis of RCC, up to date, parameters such as pathologic stage, the presence of micro-invasion, histological sub-type, nuclear atypia degree, specific clinical symptoms and findings have been used [2,17]. But, these parameters are determined generally during pathological examination and is unable to give sufficient information to clinician in predicting tumor act before nephrectomy [2]. Today, still, a tumor marker used for diagnosis of RCC, post-surgery follow-up, giving important information to clinician, and used routinely has been unable to be defined [2]. In the literature, although various tumor indicators (Ferritin, Telomerase-related protein I, Haptoglobin, Plasma fibrinogen, Carcinoembryogenic antigen, Erythropoietin, Erythrocyte sedimentation rate, C-reactive protein, Basic fetoprotein, alpha-1 antitrypsin, Renin etc.) used for diagnosis and follow-up of RCC have been described, efficacy and clinical usage of these factors are limited [2,18-21]. Therefore, effective markers that can be used in diagnosis, staging, and clinical follow-up of RCC are needed. Recently, Mean Platelet Volume (MPV) have become a research subject in cancer patients. In our study too, the association between MPV and RCC was evaluated.

Mean platelet volume (MPV) is a simple indicator showing thrombocyte function and activation and can be affected by inflammation and noted with hematologic tests [7]. In cases such as chronic hypoxia such as nasal septal deviation and sleep apnea syndrome, MPV has been reported to increase [15,22]. Additionally, in vascular events such as myocardial infarct, acute ischemic stroke, venous thromboembolism, arterial thrombosis and in Type II diabetes mellitus, the MPV values increase [12-14]. On the other hand, the MPV values have been reported to decrease in rheumatoid arthritis, ankylosing spondylitis, and inflammatory bowel diseases [7,23,24].

In cancer patients, the risk of thromboembolism increases. Due to the risk of ischemia and thrombosis, MPV values have become a research subject in patients with cancer. In the literature, no study about MPV values in renal carcinomas has been encountered. However, studies researching the association between other organ cancers and MPV values are present. Mutlu *et al.* have reported that MPV values were found lower in patients with colon cancer [25]. Nonetheless, in the study performed by Karaman *et al.*, they have reported that MPV values in patients with pancreatic adenocarcinoma is higher than patients with pancreatic neuroendocrin tumor [7].

In the literature, different results related to MPV values in cancer patients have been reported. In our study, mean MPV values was observed to elevate, as long as grade in renal cell carcinomas increases; however, statistically no significant difference was determined. Through studies to be performed on the larger series, clearer results can be achieved in direction of change in MPV values and that it can be used as

a tumor indicator in patients with renal cell carcinoma.

5. Conclusion

In non-metastatic operable renal cell carcinomas, the markers which will be a precursor of clinical and pathologic stage of tumor may be a guide for a clinician. In our study, a positive correlation was observed to be between meant MPV values and tumor grade. However, statistically no significant difference was determined. It can be supported with the larger series that MPV for renal tumors, that is rapidly and expansively growing tumor, can be an effective biochemical indicator in early diagnosis, staging, and evaluation of response to treatment

Conflict of interest

The authors declare no conflict of interest.

References

- [1] Jemal A, Siegel R, Ward E, *et al.* Cancer statistics, 2008. *CA Cancer J Clin* 2008; 58:71-96.
- [2] Erdemir F, Parlaktas BS, Uluocak N, Ozcan F, Celik M, Gokce O. The significance of serum ferritin level in renal cell carcinoma. *Turk J Urol* 2005; 31 (4): 479-484.
- [3] Gogus C, Baltaci S, Filiz E, Elhan A, Beduk Y: Significance of thrombocytosis for determining prognosis in patients with localized renal cell carcinoma. *Urology* 2004; 63: 447- 450.
- [4] Van Poppel H. Conservative vs radical surgery for renal cell carcinoma. *BJU Int* 2004; 94: 766-768.
- [5] Ali MA, Akhmedkhanov A, Zeleniuch-Jaquotte A, Toniolo P, Frenkel K, Huang X. Reliability of serum iron, ferritin, nitrite, and association with risk of renal cancer in women. *Cancer Detect Prev* 2003; 27: 116-121.
- [6] Miyata Y, Koga S, Nishikido M, Hayashi T, Kanetake H. Relationship between serum ferritin levels and tumor status in patients with renal cell carcinoma. *BJU Int* 2001; 88: 974-977.
- [7] Karaman K, Bostanci EB, Aksoy E, *et al.* The predictive value of mean platelet volume in differential diagnosis of non-functional pancreatic neuroendocrine tumors from pancreatic adenocarcinomas. *Eur J Intern Med* 2011; 22: 95-98.
- [8] Cil H, Yavuz C, Islamoglu Y, *et al.* Platelet Count and Mean Platelet Volume in Patients With In-Hospital Deep Venous Thrombosis. *Clin Appl Thromb Hemost* 2012; 18(6): 650-3.
- [9] Kamath S, Blann AD, Lip GY. Platelet activation: assessment and quantification. *Eur Heart J* 2001; 22:1561-1571.
- [10] Park Y, Schoene N, Haris W. Meanplateletvolume as an indicator ofplateletactivation: methodologicalissues. *Platelets* 2002; 13:301-306.
- [11] Tsiara S, Elisaf M, Jagroop IA, *et al.* Platelets as predictors ofvascular risk: is there a practicalindex of plateletactivity? *Clin Appl Thromb Hemost* 2003; 9:177-190.

- [12] Martin JF, Shaw T, Heggie J, et al. Measurement of the density of platelets and its relationship to volume. *Brit J Haematol* 1983; 54:337-352.
- [13] Bath PM, Butterworth RJ. Platelet size: Measurement, physiology and vascular disease. *Blood Coagul Fibrin* 1996; 7:157-161.
- [14] Butterworth R, Bath P. The relationship between mean platelet volume, stroke subtype and clinical outcome. *Platelets* 1998; 9: 359-364.
- [15] Varol E, Ozturk O, Gonca T, et al. Mean platelet volume is increased in patients with severe obstructive sleep apnea. *Scand J Clin Lab Invest* 2010;70: 497-502.
- [16] Cookson MS: Glenn's Urologic Surgery. Fifth edition. Chapter 7, 61-77, 1998.
- [17] Gelb AB: Renal cell carcinoma: Current prognostic factors. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer* 1997; 80: 981-986.
- [18] Kokocinska D, Rajchel K, Nalewajka E, Zagalski K. The usefulness of serum levels of CEA, CA 50, and ferritin in the management of renal cell cancer. *J Environ Pathol Tox Oncol* 1996; 15: 279-281.
- [19] Citterio G, Bertuzzi A, Tresoldi M, et al. Prognostic factors for survival in metastatic renal cell carcinoma: Retrospective analysis from 109 consecutive patients. *Eur Urol* 1997; 31: 286- 291.
- [20] Dexeus FH, Logothetis CJ, Sella A, et al. Serum biomarkers in metastatic renal cell carcinoma. *Urology* 1991; 38: 6-10.
- [21] Kirkali Z, Guzelsoy M, Mungan MU, Kirkali G, Yorukoglu K. Serum ferritin as a clinical marker for renal cell carcinoma: Influence of tumor size and volume. *Urol Int* 1999; 62: 21-25.
- [22] Sagit M, Korkmaz F, Kavugudurmaz M, Somdas MA. Impact of Septoplasty on Mean Platelet Volume Levels in Patients With Marked Nasal Septal Deviation. *J Craniofac Surg* 2012; 23: 974-976.
- [23] Gasparyan AY, Ayyazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Design* 2011;17: 47-58.
- [24] Khandekar MM, Khurana AS, Deshmukh SD, Kakrani AL, Katdare AD, Inamdar AK. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. *J Clin Pathol* 2006; 59: 146-149.
- [25] Mutlu H, Berk V, Karaca H, Erden A, Aslan T, Akca Z. Treatment Regimen With Bevacizumab Decreases Mean Platelet Volume in Patients With Metastatic Colon Cancer. *Clin Appl Thromb Hemost* 2012; Sep 1: 546-548.