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Are measuring CA-125 and RDW in stage III and IV endometriosis helpful for operative planning?

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ABSTRACT

Introduction: The aim of this study was to assess the expression of CA-125 (cancer antigen-125) and RDW (red cell distribution width) levels in patients with endometriosis and to compare these biomarkers in stage III and IV of the disease in order to arrange

operative planning. *Methods:* This retrospective study was conducted on a sample of women with surgical diagnosis of endometriosis. Surgical reports and laboratory tests were recorded from medical files. According to the American Society for Reproductive Medicine, patients were divided into two groups, stage III and stage IV. Preoperative serum level of CA-125 and RDW were recorded. Then, we analyzed the data using logistic regression analysis to assess the association between the disease stage and these biomarkers. *Results:* In all the data, 183 patients were available for analysis (96 patients with stage III and 87 patients with stage IV). The comparison between patients with stage III and IV showed that the mean levels of CA-125 and RDW were significantly lower in stages III patients, respectively (58.16 vs. 95.86, P < 0.0001; and 13.11 vs. 13.78, P = 0.007). The association between stage and these biomarkers as assessed by performing logistic regression analysis indicated that patients with stage IV were more likely to present with elevated levels of CA-125 (OR=1.01, 95% CI: 1.00-1.02) and RDW (OR=1.37, 95% CI: 1.09-1.74). *Conclusion:* The findings suggest that CA-125 and RDW can predict the severity of endometriosis and clinicians can use these biomarkers in addition to physical examination and ultrasound for operative planning.

Keyword: endometriosis, RDW, CA-125, biomarker, severity

1. INTRODUCTION

Endometriosis is defined as an estrogen dependent disease with presence of endometrial glands and stroma in ectopic location including the ovaries, recto-vaginal space, and peritoneum (Vercellini, 2014 and Giudice LC, 2010). The prevalence of endometriosis is 10-15% in reproductive age women and 20-48% among infertile females (Mowers, 2016; Hirsch, 2015). The diagnosis might be confirmed with a mean latency of 7-11 years from the onset of symptoms. Thus, the prevalence may be underestimated (Hirsch, 2016; Staal, 2016).

Definite diagnosis of endometriosis is achieved by laparoscopy and histopathology of the removed tissue (Hickey, 2014). However, the European Society of Human Reproductive and Embryology (ESHRE) indicated that the disease can be diagnosed only by seeing during laparoscopy by experienced surgeons (Dunselman, 2014). The endometriosis mapping before curative surgery is very important (Hirsch M, 2016). Therefore, non-invasive procedure should be studied for screening or assessing the disease severity.

Although there are no reliable blood tests for the diagnosis of endometriosis (May K, 2010), there is evidence that patients with endometriosis present with high levels of CA-125 in peripheral blood and that it can be used for prediction of the advanced endometriosis (Nisenblat, 2016; Ozhan, 2014; Kurdoglu, 2009; Shen, 2015). Different cut-off values for CA125 levels with different sensitivity and specificity are suggested (Nisenblat, 2016; Speer, 2017; Hirsch, 2017). For instance, a study showed that CA-125 at different thresholds, demonstrating the following mean sensitivities and specificities for diagnosis of endometriosis: for cut-off > 10.0 to 14.7 U/ml: 0.70 and 0.64; for cut-off > 16.0 to 17.6 U/ml: 0.56 and 0.91; for cut-off > 20.0 U/ml: 0.67 and 0.69; for cut-off > 25.0 to 26.0 U/ml: 0.73 and 0.70; for cut-off > 30.0 to 33.0 U/ml: 0.62 and 0.76; and for cut-off > 35.0 to 36.0 U/ml: 0.40 and 0.91 (Nisenblat, 2016).

In addition to CA-125, a novel serum marker known as the Red Blood Cell Distribution Width (RDW) also is found to be associated with severity of endometriosis. It has been suggested that RDW can be measured as a noninvasive simple test for detection of severity of endometriosis (Kurt, 2014). However, a few studies exist that investigate the relationship between these markers and endometriosis (Kim, 2014; Burney, 2012).

The aim of the present study was to assess preoperative blood CA-125 and RDW in endometriosis and to evaluate the association between advanced stages of endometriosis and these blood tests. It was hoped that the findings from the current investigation could contribute to the existing literature and perhaps use the results for improving clinical practice.

2. MATERIAL AND METHODS

Design and procedure

This was a retrospective study of a sample of women with confirmed diagnosis of endometriosis. The inclusion criteria included stages III and IV endometriosis that was surgically reported with visual diagnosis and was pathologically confirmed. The exclusion criteria included pregnancy, leiomyoma, adenomyosis, anemia, pelvic inflammatory disease, and chronic diseases or drugs that could have potential influence on laboratory tests. To collect data, the following information was extracted from medical case records: age, CA-125, RDW, stages of endometriosis, and cyst size.

Measures

The CA125 level was measured with Immullite 2000 (u/ml) and RDW was measured with Cell Counter.

Statistical analysis

Descriptive statistics was used to explore the data. We used the nonparametric tests (Mann-Whitney) for comparison. We performed logistic regression analysis in order to assess the relationship between stages of endometriosis and blood markers. We calculated odds ratios for independent variables including age, CA-125, RDW, right and left ovarian cyst size in predicting stage IV of the disease.

3. RESULTS

In all 215 women with confirmed diagnosis of endometriosis were approached. Of these 32 patients were excluded due to the following reasons: 25 patients due to diagnosis of leiomyoma and adenomyosis, 5 patients due to anemia, and 2 patients due to PID. Finally, the data for 183 patients were available for analysis. According to the American Society for Reproductive Medicine (ASRM), patients were divided into two groups: patients with stage III (n = 96, 52.5%) and cases with stage IV (n = 87, 47.5%). The characteristics for patients in two groups are shown in Table 1. In addition the mean CA-125 and RDW levels are depicted in Figure 1.

Table 1 Comparison between stages III and IV of endometriosis derived from Mann-Whitney u test

	All	Stage III (n=96)	Stage IV (n=87)	
	Mean± SD	Mean± SD	Mean± SD	P
Age	30.5 (6.73)	30.1 (7.26)	31.0 (6.11)	0.16
CA125	76.0 (67.3)	58.1 (47.84)	95.8 (79.37)	<0.0001
RDW	13.4 (1.51)	13.1 (1.12)	13.7 (1.79)	0.007
Left cyst size	4.0 (3.21)	3.4 (3.24)	4.7 (3.03)	0.003
Right cyst size	3.7 (3.58)	3.1 (3.68)	4.5 (3.33)	0.005

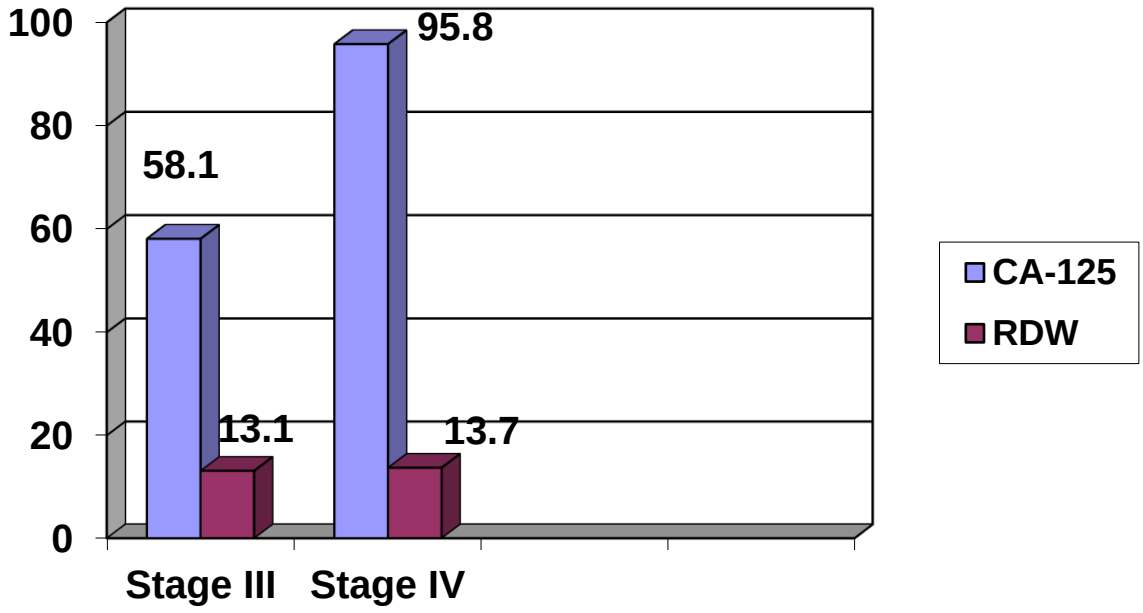

Figure 1 The mean CA-125 and RDW levels by disease stage

The association between blood markers and stage of the disease is presented in Table 2. The results obtained from logistic regression analysis indicated that both CA-125 (OR = 1.009, 95% CI = 1.002-1.015) and RDW (OR = 1.317, 95% CI = 1.031-1.683) were associated with advanced stage of the disease. Indeed, the association of RDW compared to CA-125 was marked.

Table 2 The association between independent variables and the disease stage (stage IV and Stage III)

	OR* (95%CI)	P value
Age	0.99 (0.97-1.01)	0.303
CA125	1.01 (1.00-1.02)	0.008
RDW	1.31 (1.03-1.68)	0.027
Right ovary size	1.27(1.12-1.44)	<0.0001
Right ovary size	1.35(1.12-1.56)	<0.0001

Odds ratio for Stage IV

4. DISCUSSION

Endometriosis is known as a multi-factorial disease with inflammatory process. The cytokines, chemokines, and prostaglandins release in ectopic endometrial tissue in women with endometriosis significantly (Ozhan, 2014; Burney, 2012). The obvious biomarker of endometriosis includes CA-125 that can be associated with sever endometriosis (Hirsch, 2015; Kurdoglu, 2009; Masahashi, 1988; Harada, 2002). Similarly, we found that compared to the stages III, CA-125 was higher in patients with stage IV of the disease.

The Red cell distribution width (RDW) is defined as a biomarker associated with anemia (Weiss, 2005). Recently, RDW has been shown to be related to inflammation. Inflammation reduces the life span of erythrocytes via impairing iron metabolism and response to erythropoietin leads to increase in RDW levels (Özcan, 2013). Lippi et al. showed that RDW has a significant correlation with hsCRP and sedimentation which both are known as inflammatory markers (Lippi, 2009). However, as indicated here RDW was higher in stage IV of the disease compared to stage III. A relatively similar findings was reported by Kurt et al. where the found a significant different levels of RDW between sever and moderate endometriosis (Kim, 2014). The association between endometriosis and RDW can be explained by the increased inflammatory markers due to retrograde menstruation theory (Seli, 2003; Ahn, 2017).

This was a small-scale study and thus the findings should be interpreted with caution. It seems that further studies are needed to establish stronger evidence for the relationship between CA-125 and RDW and the stage of endometriosis so that gynecologist and obstetricians could provide better care for these patients.

5. CONCLUSION

The findings suggest that CA-125 and RDW can predict the severity of endometriosis and clinicians can use these biomarkers in addition to physical examination and ultrasound for operative planning. Perhaps using CA-125 and RDW in this context could improve outcomes and make operative planning more accurate.

Authors Contributions

ZT make substantial contributions to conception and design, analysis and interpretation of data, and drafting the article. JZ have contributed to acquisition of data and analysis of data. FT contributes to the valuable suggestion and consultation in preparing article. AM participate in revising it critically for important intellectual content. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

The study was approved by the Tehran University of Medical Science (IR.TUMS.MEDICINE.REC.1397.595). All research activities were performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Conflict of interests

The authors declare that they have no competing interests.

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