original article

Preoperative thrombocytosis as a prognostic factor in endometrioid-type endometrial carcinoma

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BACKGROUND: The impact of preoperative thrombocytosis as a prognostic factor in endometrial carcinoma (EC) remains uncertain and has never been examined in Saudi Arabia.
OBJECTIVES: To determine the prevalence of preoperative thrombocytosis (platelet count >400 000/μL), and its prognostic significance for clinicopathological factors and survival in Saudi patients with endometrioid-type EC.
DESIGN: A retrospective cross-sectional study from January 2010 to December 2013.
SETTING: A referral tertiary healthcare institute.
PATIENTS AND METHODS: Patients who underwent staging surgery for primary endometrioid-type EC were retrospectively analyzed for perioperative details: age, preoperative platelet count, International Federation of Gynecology and Obstetrics (FIGO) stage, endometrioid grade, recurrence, disease-free survival (DFS) and overall survival (OS). Survival analysis was conducted using Kaplan-Meier estimates and a Cox proportional hazards model.
MAIN OUTCOME MEASURES: Prevalence of preoperative thrombocytosis, DFS and OS.
RESULTS: In 162 patients who met inclusion criteria, the frequency of preoperative thrombocytosis was 8.6% (n=14). Patients with advanced FIGO disease (stages III-IV) and recurrence had significantly higher mean preoperative platelet counts than patients with early FIGO disease (stages I-II) and no recurrence (P=.0080 and P=.0063, respectively). Patients with thrombocytosis had statistically significant higher rates of advanced FIGO stages III–IV disease, unfavorable grades II–III endometrioid histology and recurrence than patients with preoperative platelet counts ≤400 000/μL (P<.001, P<.0105 and P<.001, respectively). In a univariate analysis, patients with preoperative thrombocytosis had statistically lower mean DFS and OS rates than patients without thrombocytosis (P<.0001 and P<.0001, respectively). In a multivariate analysis, thrombocytosis was not an independent prognostic factor of DFS and OS.
CONCLUSION: The frequency of preoperative thrombocytosis is not uncommon. Also, preoperative thrombocytosis is associated with poor clinicopathological prognostic factors, and poor survival outcomes in a univariate but not multivariate analysis.
LIMITATION: The retrospective study design, sample size and lack of exploration of other clinicopathological factors.

Endometrial carcinoma (EC) is the most frequent gynecologic cancer in developed countries and the second most frequent gynecologic cancer in developing countries.[1] Several important prognostic factors in EC include: the International Federation of Gynecology and Obstetrics (FIGO) stage, histologic subtype, histologic grade, depth of myometrial invasion and lymphovascular space invasion.[2,3] The few

studies of preoperative thrombocytosis as a prognostic factor have shown that preoperative thrombocytosis was associated with other poor prognostic factors and survival outcomes in patients with EC.[4-15] To the best of our knowledge, no study of preoperative thrombocytosis has been conducted in Saudi Arabia. Our retrospective study had three aims: 1) determine the prevalence of preoperative thrombocytosis, 2) explore the relationship between preoperative thrombocytosis and several clinicopathological prognostic factors (FIGO stage, endometrioid grade and recurrence), and 3) investigate the survival impact of preoperative thrombocytosis on disease-free survival (DFS) and overall survival (OS) in Saudi patients with endometrioid-type EC.

PATIENTS AND METHODS

The study took place at King Faisal Specialist Hospital & Research Centre (KFSH&RC), Riyadh, Saudi Arabia—a referral tertiary healthcare institute. The study protocol was approved by the Research Advisory Council (RAC) and Institutional Review Board (IRB) at KFSH&RC, Riyadh, Saudi Arabia (ID: 2161 094).

From January 2010 to December 2013, all patients who underwent staging surgery for primary EC were retrospectively analyzed for perioperative details (n=254). Staging surgeries were total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal cytology and pelvic and para-aortic lymphadenectomy.[16] Perioperative details included age, preoperative platelet count, FIGO stage, endometrioid histologic grade, recurrence, DFS and OS. In all cases, preoperative platelet counts were obtained within 2 days before surgery, and evaluated by conventional automated flow cytometry hematology analyzers. Consistent with previous studies, thrombocytosis was defined as platelet count more than 400 000/μL.[4,5,7-11,13] After review of the histologic slides of all surgical specimens, FIGO stage was determined according to the 2009 FIGO staging system.[17] The histological classification of EC was based on World Health Organization classification of tumors.[18] Only patients with endometrioid-type ECs were included in the study analysis. Endometrioid tumors were graded as follows: well (grade I), moderately (grade II) and poorly (grade III) differentiated tumors according to the FIGO grading system. Recurrence was evaluated based on clinical, laboratory and imaging tests. DFS was calculated from the day of surgery to the time of local/distant disease progression or last date of follow-up, whichever came first. OS was calculated from the day of surgery to the time of death or last date of follow-up, whichever came first.

Exclusion criteria included non-endometrioid histology, missing preoperative platelet count, preoperative platelet count obtained more than 2 days before the surgery, preoperative neoadjuvant chemotherapy, incompletely staged surgery and conditions associated with thrombocytosis (for example, second malignancies, hematological diseases, inflammatory conditions, drug-related side effects and others).

All patients were followed up regularly at the outpatient clinic. The follow-up work-up included routine physical examination and vault smear. Chest X-ray, whole-body computed tomography (CT) scan, and positron emission tomography/CT scan were done as clinically appropriate.

Age (<50 years vs. ≥50 years), FIGO stage (I-II vs. III-IV), endometrioid histologic grade (I vs. II-III), recurrence (no vs. yes) and preoperative platelet count (≤400 000/μL vs. >400 000/μL) were dichotomized into two groups. In the study, endometrioid histologic grade I was considered favorable whereas endometrioid histologic grades II-III were considered unfavorable.[4,5,7] Numerical data are presented as mean, standard deviation, and range. Categorical data are presented as number of cases (n) and percentages (%). Two-tailed Mann-Whitney U test and chi-square tests were used for univariate analyses. Survival analyses for disease-free survival (DFS) and overall survival (OS) were calculated by the Kaplan-Meier estimates method and compared by using a two-tailed log-rank test. Univariate and multivariate analyses of survival were performed using the Cox proportional hazards model. All statistical analyses were performed using IBM SPSS software version 22 for Windows (IBM Corp, Armonk, NY). *P* values <.05 were regarded as statistically significant.

RESULTS

Of 254 patients who underwent surgery, 162 patients met the inclusion criteria. The mean (SD) age was 59 (11) years (range: 31–95 years) **(Table 1)**. The overall mean preoperative platelet count was 293 000 (87 000) (range: 91 000 – 615 000). The frequency of preoperative thrombocytosis was 8.6% (n=14). Early FIGO disease (stages I-II) and advanced FIGO disease (stages III–IV) were present in 129 (79.6%) and 33 patients (20.4%), respectively. Favorable low grade (grade I) endometrioid histology was present in 76 patients (46.9%) whereas combined unfavorable intermediate and high grade (grades II–III) endometrioid histology was present in 86 patients (53.1%). Twenty-three patients (14.2%) developed recurrence after surgery.

In the univariate analysis of mean preoperative platelet count and clinicopathological factors, patients with advanced FIGO disease (stages III–IV) and recur-

rence had significantly higher mean preoperative platelet counts when compared to patients with early FIGO disease (stages I–II) and no recurrence (*P*=.0080 and *P*=.0063, respectively) **(Table 2)**. In the univariate analysis between preoperative platelet count and clinicopathological factors, patients with thrombocytosis had statistically higher rates of advanced FIGO stage III–IV disease (*P*<.001), unfavorable grades II–III endometrioid histology (*P*<.0105) and recurrence (*P*<.001) than patients with preoperative platelet counts less than 400 000/μL **(Table 3)**. In the univariate analyses of DFS and OS using the Cox proportional hazards model, age was not an independent prognostic factor of DFS and OS **(Table 4)**. However, preoperative platelet count, FIGO stage and endometrioid grade were independent prognostic factors of DFS (*P*<.0001, *P*<.0001 and *P*<.0001, respectively) and OS (*P*<.0001, *P*<.0001 and *P*=.0003, respectively).

Univariate Kaplan-Meier survival curves for mean DFS and OS rates according to the preoperative platelet counts are shown in **Figures 1 and 2**, respectively. Patients with thrombocytosis had lower statistically significant mean DFS and OS rates than patients without thrombocytosis (1.7 [0.3] vs. 5.2 [0.1] years, *P*<.0001 and 2.0 [0.2] vs. 5.4 [0.1] years, *P*<.0001, respectively). In the multivariate analyses of DFS and OS using the Cox proportional hazards model, preoperative platelet count was an independent prognostic factor of DFS and OS **(Table 5)**. However, FIGO stage, endometrioid grade and age were independent prognostic factors of DFS (*P*<.0001, *P*=.0189 and *P*=.0480, respectively) and OS (*P*<.0001, *P*=.0017 and *P*=.0172, respectively).

DISCUSSION

The clinical relationship between thrombocytosis and malignancy was first documented in 1972 by Riess.[19] The precise underlying pathogenesis of thrombocytosis in the setting of malignancy remains poorly defined.[13] However, increased concentrations of tumor-related humoral factors, mainly thrombopoietin (TPO) and interleukin-6 (IL-6), have been proposed as plausible etiologies for the underlying reactive thrombocytosis.[13] IL-6 is a potent stimulator of megakaryocytopoiesis, and it has been demonstrated that tumor cells produce IL-6 in in-vivo[20] and in-vitro[21] studies. TPO, which is mediated by IL-6 stimulation and produced by the liver, is a crucial hormone implicated in the differentiation of platelet precursors (megakaryocytes) into the mature blood thrombocytes (platelets).[22] However, studies of IL-6 concentrations in patients with EC have been contradictory. Chopra and colleagues[23] documented

Table 1. Characteristics of patients with endometrioid-type endometrial carcinoma (n=162).

Characteristic	Data
Age (years) including range	59 (11) (31-95)
<50 years	32 (19.8)
≥50 years	130 (80.2)
Mean preoperative platelet count (SD) (range)	293 000 (87 000) (91 000-615 000)
Preoperative platelet count	
≤400 000/μL, n (%)	148 (91.4)
>400 000/μL, n (%)	14 (8.6)
FIGO Stage	
I-II	129 (79.6)
III-IV	33 (20.4)
Endometrioid grade	
I	76 (46.9)
II-III	86 (53.1)
Recurrence	
No	139 (85.8)
Yes	23 (14.2)

Data are mean (standard deviation) or number (percentage). FIGO: International Federation of Gynecology and Obstetrics

Table 2. Univariate analysis of mean preoperative platelet count/μl and clinicopathological factors (age, FIGO stage, endometrioid grade and recurrence) in patients with endometrioid-type endometrial carcinoma (n=162).

Variable	n (%)	Mean preoperative platelet count/μL	Univariate, *P* value
Age			
<50 years	32 (19.8)	299 000	.3222
≥50 years	130 (80.2)	292 000	
FIGO Stage			
I–II	129 (79.6)	282 000	.0080
III–IV	33 (20.4)	337 000	
Endometrioid grade			
I	76 (46.9)	288 000	.6171
II–III	86 (53.1)	298 000	
Recurrence			
No	139 (85.8)	285 000	.0063
Yes	23 (14.2)	348 000	

FIGO: International Federation of Gynecology and Obstetrics. Statistical analysis by two-tailed Mann-Whitney U test.

Table 3. Univariate association between mean preoperative platelet count/µl and clinicopathological factors (age, FIGO stage, endometrioid grade and recurrence) in patients with endometrioid-type endometrial carcinoma (n=162).

Variable	Mean preoperative platelet count/µl		Univariate, *P* value
	Normal platelet count (≤400 000/µl) n=148	Thrombocytosis (>400 000/µL) n=14	
Age			
<50 years	30 (93.8)	2 (6.2)	.5909
≥50 years	118 (90.8)	12 (9.2)	
FIGO Stage			
I–II	126 (97.7)	3 (2.3)	.001
III–IV	22 (66.7)	11 (33.3)	
Endometrioid grade			
I	74 (97.4)	2 (2.6)	.0105
II-III	74 (88.1)	12 (11.9)	
Recurrence			
No	133 (95.7)	6 (4.3)	.0001
Yes	15 (65.2)	8 (34.8)	

Data are number (percentage). Statistical analysis by chi-square test. FIGO: International Federation of Gynecology and Obstetrics

Table 4. Univariate analyses of disease-free survival and overall survival using Cox proportional hazards model with clinicopathological factors in patients with endometrioid-type endometrial carcinoma (n=162).

	Disease-free survival (years)	*P* value	Overall survival (years)	*P* value
Preoperative platelet count				
≤400 000/µl (n=14)	5.23 (0.15)	<.0001	5.40 (0.13)	<.0001
>400 000/µl (n=148)	1.69 (0.27)		2.00 (0.22)	
FIGO Stage				
I-II (n=129)	2.62 (0.43)	<.0001	3.65 (0.49)	<.0001
III-IV (n=33)	2.29 (0.04)		2.31 (0.04)	
Endometrioid grade				
I (n=76)	5.66 (0.13)	<.0001	5.77 (0.11)	.0003
II-III (n=86)	2.71 (0.14)		2.89 (0.12)	
Age				
<50 years (n=32)	3.32 (0.16)	.5976	2.77 (0.05)	.1419
≥50 years (n=130)	5.00 (0.18)		5.15 (0.17)	

Data are mean (standard deviation) . Statistical analysis by two-tailed log-rank test. FIGO: International Federation of Gynecology and Obstetrics

no elevated IL-6 concentrations, whereas Scambia and partners[24] documented elevated IL-6 concentrations in only 37% of patients with EC. The exact pathophysiology of thrombocytosis in EC is an interesting field for further exploration.

Few studies have examined the significance of preoperative thrombocytosis as a prognostic factor in EC.[4-15] **Table 6** summarizes the existing literature on preoperative thrombocytosis (platelet count >400 000/µL) as a prognostic factor in patients with EC. Thus far, no single strong-evidence systematic analysis/meta-analysis study has been conducted to examine the prevalence and significance of preoperative thrombocytosis in patients with EC — this is an important direction for future research. Moreover, the available data are inconsistent with regard to definition of thrombocytosis, study sample size, study design, status of complete staging surgery, statistical calculations and inconsistent findings. However, almost all studies indicate that preoperative thrombocytosis is a poor prognostic marker in patients with EC.

In our study, the prevalence of thrombocytosis was 8.6%. Earlier studies demonstrated that the prevalence of thrombocytosis (defined as platelet count >400 000/µL) ranged from as low as 1.5% to as high as 18.2% in patients with EC.[4,5,7-11,13]

Moreover, in our study, advanced FIGO disease (stages III-IV), but not tumor grade, was associated with higher mean preoperative platelet counts than patients with early FIGO disease (stages I-II). Our findings mirrored previous studies reported elsewhere by Gorelick et al.,[10] Njolstad et al.[12] and Heng et al.[13] On the other hand, Ayhan and colleagues evaluated preoperative platelet count in a total of 155 patients with endometrial carcinoma.[8] They found that both advanced FIGO disease (stages III-IV) and poorly differentiated tumor (grade III) were associated with significantly higher median preoperative platelet counts when contrasted with early FIGO disease (stages I-II) and well differentiated tumor (grade I). Metindir and partners examined the association between preoperative hemoglobin and platelet count as prognostic factors in a sum of 61 patients with EC.[11] They found no significant correlation between median preoperative platelet counts and grade of EC; FIGO stage was not examined in the univariate analysis of median preoperative platelet counts.

Further, our data show that patients with thrombocytosis have significantly higher rates of advanced FIGO disease (stages III-IV), unfavorable grade histology (grades II-III) and recurrence than patients without thrombocytosis. Our results are similar to the study reported by Gucer et al.,[5] and inconsistent with the

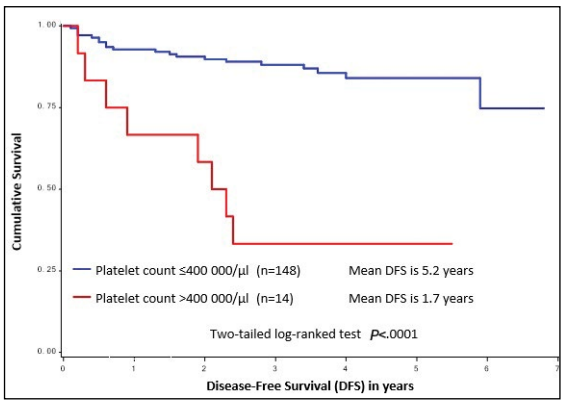

Figure 1. Kaplan-Meier survival curve for mean disease-free survival (DFS) by the preoperative platelet count in patients with endometrioid-type endometrial carcinoma (n=162).

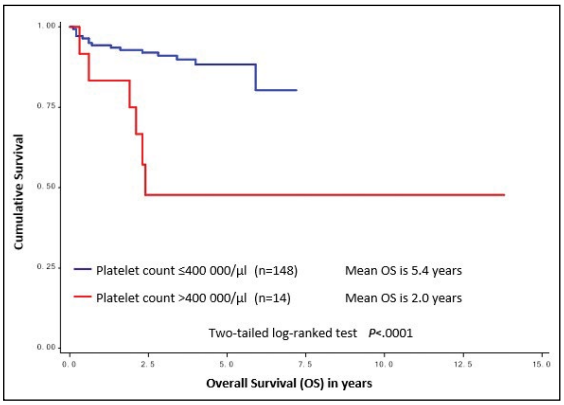

Figure 2. Kaplan-Meier survival curve for mean overall survival (OS) by the preoperative platelet count in patients with endometrioid-type endometrial carcinoma (n=162).

Table 5. Multivariate analyses of disease-free survival and overall survival using Cox proportional hazards model with clinicopathological factors in patients with endometrioid-type endometrial carcinoma (n=162).

	Disease-free survival			Overall survival		
	***P* value**	**Hazard ratio**	**95% CI**	***P* value**	**Hazard ratio**	**95% CI**
Preoperative platelet count						
≤400 000/µl (n=148)	.0535	2.382	0.987 – 5.748	.2451	1.786	0.672 – 4.746
>400 000/µl (n=14)						
FIGO Stage						
I-II (n=129)	<.0001	2.827	2.013 – 3.972	<.0001†	2.389	1.622 – 3.518
III-IV (n=33)						
Endometrioid grade						
I (n=76)	.0189	1.848	1.107 – 3.085	.0017†	2.914	1.495 – 5.678
II-III (n=86)						
Age						
<50 years (n=32)	.0480	1.032	1.000 – 1.065	.0172†	1.043	1.007 – 1.079
≥50 years (n=130)						

Two-tailed log-rank test
FIGO: International Federation of Gynecology and Obstetrics

study reported by Kaloglu et al.[14] which showed that thrombocytosis (defined as preoperative platelet count ≥300 000/µl) was not correlated with stage and grade of EC. Among patients with EC and preoperative thrombocytosis (>400 000/µl), Heng and colleagues[13] found higher rates of advanced FIGO disease (stages III-IV) whereas Ayhan and partners[8] found higher rates of unfavorable grade histology (grades II-III).

In univariate analysis, our results demonstrated that thrombocytosis was associated with significantly lower mean DFS and OS rates than patients without thrombocytosis. Similar findings were echoed in earlier studies which showed that patients with thrombocytosis had significantly lower 5-year DFS[5,6,10,13] and 5-year OS[5,6,10,12,13] rates than patients without thrombocytosis.

In multivariate analysis, our results demonstrated that thrombocytosis was not an independent poor prognostic factor of DFS and OS. Possible reasons our results differ from others can be attributed to the sample size and methodological issues in defining the cat-

Table 6. Summary of published reports on preoperative thrombocytosis (platelet count >400 000/μL) as a prognostic factor in patients with endometrial carcinoma.

Reference	Authors	Year	Country	n	Summary
4	Menczer et al.	1996	Israel	66	Prevalence of thrombocytosis was 1.5% (n=1) Thrombocytosis was associated with unfavorable grade (II-III) Elevated platelet count was associated with poor survival rate, and an insignificantly higher prevalence of older age, high stage and deep myometrial invasion
5	Gucer et al.	1998	Austria	135	Prevalence of thrombocytosis was 14% (n=19) Thrombocytosis was associated with advanced FIGO stage (II-IV), poor histologic grade (II-III), deep myometrial invasion, lymphovascular space invasion, higher 5-year recurrence and lower 5-year OS rates In multivariate analysis, thrombocytosis, grade, age and stage were significantly associated with poor survival
6	Scholz et al.	2000	Austria	59	Prevalence of thrombocytosis was 20.3% (n=12) in patients with stage III-IV Thrombocytosis was associated with lower 5-year DFS and OS rates In multivariate analysis, 5-year DFS and OS were influenced significantly by FIGO stage (III vs. IV), thrombocytosis and cervical involvement
7	Tamussino et al.	2001	Austria	212	Prevalence of thrombocytosis was 12.7% (n=27) The rate of thrombocytosis was significantly higher in patients with a hemoglobin level <12.0 g/dL than in those with a hemoglobin level >12.0 g/dL Thrombocytosis with anemia (12.0 g/dl) was associated with advanced FIGO stage, poor histologic grade (II-III) and non-endometrioid histology. In multivariate analysis, age, thrombocytosis, non-endometrioid histology, high-grade histology and advanced FIGO stage were significantly associated with poor prognosis
8	Ayhan et al.	2006	Turkey	155	Prevalence of thrombocytosis was 7.7% (n=12) Advanced stage (III-IV), poorly differentiated tumor grade (grade III), the presence of cervical and adnexal involvements were associated with significantly higher median preoperative platelet counts. Thrombocytosis was associated with higher prevalence of poor grade, endometrioid histology and positive cervical involvement
9	Lerner et al.	2007	USA	68	Prevalence of thrombocytosis was 12% (n=8) in patients with uterine papillary serous carcinomas Thrombocytosis was associated with advanced FIGO stage, ascites (>1 liter), shorter median DFS and OS In multivariate analysis, thrombocytosis was an independent poor prognostic factor

egorical variables, and interactions between categorical variables. Nevertheless, our results were consistent with two studies[11,13] and inconsistent with others.[5-7,9,10,12]

Overall, our data suggest that preoperative thrombocytosis (platelet count >400 000/μL) may be a valuable prognostic marker in patients with endometrial carcinoma. For example, preoperative thrombocytosis may identify patients who are at greater risk for advanced disease, unfavorable grade histology, recurrence and poor survival. Moreover, preoperative thrombocytosis may identify patients who require aggressive cytoreductive surgery and neoadjuvant/adjuvant treatments. Considering the reactive thrombocytosis implicated in aggressive EC, aiming at TPO and IL-6 as potential therapeutic targets is an interesting arena for future investigation.

Our study has several strengths. To the best of our knowledge, we report the first ever study from developing countries, generally, and Saudi Arabia, specifically, on the role of preoperative thrombocytosis as a prog-

Table 6 cont. Summary of published reports on preoperative thrombocytosis (platelet count >400 000/μL) as a prognostic factor in patients with endometrial carcinoma.

Reference	Authors	Year	Country	n	Summary
10	Gorelick et al.	2009	USA	77	Prevalence of thrombocytosis was 18.2% (n=14) Advanced stage (III-IV) was associated with significantly higher median preoperative platelet counts. Among patients with stages III-IV, median PFS and OS was lower in patients with thrombocytosis Among patients with stages I-II, there was no difference with respect to PFS and OS In multivariate analysis, stage and preoperative thrombocytosis were independent poor prognostic factors
11	Metindir & Bilir Dilek	2009	Turkey	61	Prevalence of thrombocytosis was 14.8% (n=9) The presence of cervical involvement and lymphatic metastasis were associated with significantly higher median preoperative platelet counts In multivariate analysis, thrombocytosis was not an independent prognostic factor
13	Heng et al.	2014	Thailand	238	Prevalence of thrombocytosis was 18.1% (n=43) Advanced stage, adnexal involvement, lymph node metastasis and positive peritoneal were significantly associated with higher mean preoperative platelet counts. Thrombocytosis was associated with advanced FIGO stage, cervical involvement, adnexal involvement, lymph node involvement, positive cytology, lower 5-year DFS and OS In multivariate analysis, thrombocytosis was not an independent prognostic factor

DFS: disease-free survival; PFS: progression-free survival; OS: overall survival; FIGO: International Federation of Gynecology and Obstetrics

nostic factor in patients with endometrioid-type EC. Moreover, our findings contribute additional data to the very scarce body of existing literature, so that generalized and solid conclusions can be deduced. Moreover, the sample size of our study is comparatively large, and all patients had uniform endometrioid-type histology and staging surgery procedures. Also, we briefly reviewed and summarized the existing literature on the topic and compared and contrasted our findings to it.

Our study has several limitations, including the retrospective study design and lack of exploration of the significance of preoperative thrombocytosis on other clinicopathological factors, such as cervical involvement, adnexal involvement and lymphovascular space invasion. These factors are going to be explored in a future study. Moreover, the platelet/lymphocyte ratio or platelet/neutrophil ratio may appear to be a better prognostic marker in EC, and this is an interesting area for prospective exploration.

In conclusion, in patients with endometrioid-type EC, the prevalence of preoperative thrombocytosis (platelet count >400 000/μL) is not uncommon. Also, preoperative thrombocytosis is associated with poor clinicopathological prognosis (predicting a more advanced cancer), and poor survival outcomes in the univariate but not the multivariate analysis.

Disclosure

The authors declare no potential conflicts of interest.

Authors' contributions

Ahmed Abu-Zaid drafted the manuscript. Ahmed Abu-Zaid, Mohannad Alsabban, Mohammed Abuzaid and Osama Alomar contributed to literature review, data collection, data analysis and data presentation in tables and figures. Osama Alomar, Hany Salem and Ismail A. Al-Badawi contributed to Institutional Review Board (IRB) paperwork, study conception, study design and supervised the research project. Ahmed Abu-Zaid, Mohannad Alsabban and Mohammed Abuzaid re-drafted the manuscript. Osama Alomar, Hany Salem and Ismail A. Al-Badawi reviewed manuscript for editorial and intellectual contents. All authors have read and approved the final draft of manuscript.

REFERENCES

1. Plaxe SC, Mundt AJ. Overview of endometrial carcinoma. In: UpToDate, Goff B, Dizon DS, Vora SR, Falk SJ (eds). UpToDate: Waltham, MA, USA; 2016. https://www.uptodate.com/contents/overview-of-endometrial-carcinoma. Accessed on December 29, 2016.
2. Prat J. Prognostic parameters of endometrial carcinoma. Hum Pathol. 2004;35(6):649-62.
3. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet. 2005;366(9484):491-505.
4. Menczer J GD, Schejter E, Zakut H. Elevated platelet count in patients with endometrial carcinoma: correlation with selected prognostic factors and with survival Int J Gynecol Cancer. 1996;6(6):463– 6
5. Gucer F, Moser F, Tamussino K, Reich O, Haas J, Arikan G, et al. Thrombocytosis as a prognostic factor in endometrial carcinoma. Gynecol Oncol. 1998;70(2):210-4.
6. Scholz HS, Petru E, Gucer F, Haas J, Tamussino K, Winter R. Preoperative thrombocytosis is an independent prognostic factor in stage III and IV endometrial cancer. Anticancer Res. 2000;20(5c):3983-5.
7. Tamussino KF, Gucer F, Reich O, Moser F, Petru E, Scholz HS. Pretreatment hemoglobin, platelet count, and prognosis in endometrial carcinoma. Int J Gynecol Cancer. 2001;11(3):236-40.
8. Ayhan A, Bozdag G, Taskiran C, Gultekin M, Yuce K, Kucukali T. The value of preoperative platelet count in the prediction of cervical involvement and poor prognostic variables in patients with endometrial carcinoma. Gynecol Oncol. 2006;103(3):902-5.
9. Lerner DL, Walsh CS, Cass I, Karlan BY, Li AJ. The prognostic significance of thrombocytosis in uterine papillary serous carcinomas. Gynecol Oncol. 2007;104(1):91-4.
10. Gorelick C, Andikyan V, Mack M, Lee YC, Abulafia O. Prognostic significance of preoperative thrombocytosis in patients with endometrial carcinoma in an inner-city population. Int J Gynecol Cancer. 2009;19(8):1384-9.
11. Metindir J, Bilir Dilek G. Preoperative hemoglobin and platelet count and poor prognostic factors in patients with endometrial carcinoma. J Cancer Res Clin Oncol. 2009;135(1):125-9.
12. Njolstad TS, Engerud H, Werner HM, Salvesen HB, Trovik J. Preoperative anemia, leukocytosis and thrombocytosis identify aggressive endometrial carcinomas. Gynecol Oncol. 2013;131(2):410-5.
13. Heng S, Benjapibal M. Preoperative thrombocytosis and poor prognostic factors in endometrial cancer. Asian Pac J Cancer Prev. 2014;15(23):10231-6.
14. Kaloglu S, Guraslan H, Tekirdag AI, Dagdeviren H, Kaya C. Relation of Preoperative Thrombocytosis between Tumor Stage and Grade in Patients with Endometrial Cancer. Eurasian J Med. 2014;46(3):164-8.
15. Ekici H, Malatyalioglu E, Kokcu A, Kurtoglu E, Tosun M, Celik H. Do Leukocyte and Platelet Counts Have Benefit for \Preoperative Evaluation of Endometrial Cancer? Asian Pac J Cancer Prev. 2015;16(13):5305-10.
16. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet. 2009;105(2):103-4.
17. Mutch DG. The new FIGO staging system for cancers of the vulva, cervix, endometrium, and sarcomas. Gynecol Oncol. 2009:115(3):325-8.
18. Silverberg SG KR, Nogales F. Tumours of the uterine corpus. In: Tavassoli FA, Devilee P (eds). World Health Organization classification of tumors. Pathology and genetics of tumours of the breast and female genital organs. IARC press: Lyon, France, 2003; pp: 221–232.
19. Riess L. Zur pathologischen anatomie des blutes. Arch Anat Physiol Wissensch Med. 1872;39:237-49.
20. Ishibashi T, Kimura H, Shikama Y, Uchida T, Kariyone S, Hirano T, et al. Interleukin-6 is a potent thrombopoietic factor in vivo in mice. Blood. 1989;74(4):1241-4.
21. Imai T, Koike K, Kubo T, Kikuchi T, Amano Y, Takagi M, et al. Interleukin-6 supports human megakaryocytic proliferation and differentiation in vitro. Blood. 1991;78(8):1969-74.
22. Kaser A, Brandacher G, Steurer W, Kaser S, Offner FA, Zoller H, et al. Interleukin-6 stimulates thrombopoiesis through thrombopoietin: role in inflammatory thrombocytosis. Blood. 2001;98(9):2720-5.
23. Chopra V, Dinh TV, Hannigan EV. Serum levels of interleukins, growth factors and angiogenin in patients with endometrial cancer. J Cancer Res Clin Oncol. 1997;123(3):167-72.
24. Scambia G, Testa U, Panici PB, Martucci R, Foti E, Petrini M, et al. Interleukin-6 serum levels in patients with gynecological tumors. Int J Cancer. 1994;57(3):318-23.