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Evaluation of Inflammatory Markers in Single-Port Laparoscopic and Vaginal Hysterectomies: A Retrospective Study in Kocaeli, Northwest Turkey

Tek Portlu Laparoskopik ve Vajinal Histerektomilerde İnflamatuar Belirteçlerin Retrospektif Değerlendirilmesi

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ABSTRACT

Objective: *The authors in this study aimed to detect inflammatory marker changes in two natural orifice hysterectomies: single-port laparoscopic hysterectomy (SLH) and vaginal hysterectomy (VH).*

Material and Methods: *Between 2018 and 2019, data obtained from patients in the SLH and VH groups were reviewed retrospectively. The preoperative and postoperative hematocrit (HCT), hemoglobin (HB), white blood cell (WBC), platelet (PLR), and neutrophillymphocyte (NLR) ratios and values were compared as well as the demographic characteristics of the patients. This study was also registered in Registry of Clinical Trials; registration number: NCT04221308.*

Results: *In the postoperative period, WBC, NLR, and PLR were statistically increased, and HB and HCT were decreased in all groups. However, the changes in inflammatory markers were similar in both groups. The changes in HB and HCT were less in the SLH group. Moreover, both the duration of the operation and the hospital stay were higher in the SLH group.*

Conclusion: *Both natural orifice techniques provided low morbidity and good cosmetic results. The results regarding inflammatory markers indicate that both procedures are acceptable. As surgical experience in performing SLH increases, operation and hospital stay durations may decrease.*

Keywords: *lymphocyte activation, natural orifice endoscopic surgery, neutrophil activation, platelet activation, vaginal hysterectomy*

ÖZET

Amaç: *Bu çalışmada iki doğal orifis histerektomide - tek portlu laparoskopik histerektomi (SLH) ve vajinal histerektomi (VH) - inflamatuar belirteç değişikliklerini saptamak amaçlanmıştır.*

Gereç ve Yöntemler: *2018-2019 arasında yapılan SLH ve VH yapılmış hastalardan elde edilen veriler retrospektif olarak incelendi. Ameliyat öncesi ve sonrası hematokrit (HCT), hemoglobin (HB), beyaz kan hücresi (WBC), trombosit (PLR) ve nötrofil-lenfosit (NLR) oranları ve değerleri ile hastaların demografik özellikleri karşılaştırıldı. Bu çalışma aynı zamanda 'Clinical Trials' a kaydedilmiştir; kayıt numarası: NCT04221308.*

Bulgular: *Postoperatif dönemde WBC, NLR ve PLR istatistiksel olarak artmış, HB ve HCT tüm gruplarda azalmıştır. Bununla birlikte, inflamatuar belirteçlerdeki değişiklikler her iki grupta da benzerdi. HB ve HCT'deki değişiklikler SLH grubunda daha azdı. Ayrıca SLH grubunda hem ameliyat süresi hem de hastanede kalış süresi daha yüksek olarak saptanmıştır.*

Sonuç: *Her iki 'doğal orifice' tekniği de düşük morbidite ve iyi kozmetik sonuçlar sağlamıştır. Enflamatuar belirteçlerle ilgili sonuçlar her iki prosedürün de kabul edilebilir olduğunu göstermektedir. SLH uygulamadaki cerrahi deneyim arttıkça operasyon ve hastanede kalış süreleri azalabilir.*

Anahtar Kelimeler: *lenfosit aktivasyonu, doğal orifis endoskopik cerrahi, nötrofil aktivasyonu, trombosit aktivasyonu, vajinal histerektomi*

INTRODUCTION

Hysterectomy is one of the most common gynecological surgical procedures worldwide [1]. It has been performed using abdominal, vaginal, and laparoscopic approaches, including robotic laparoscopic hysterectomy [2]. The superiority of laparoscopic (LH) and vaginal hysterectomies (VH) over abdominal hysterectomies (AH) has been shown in many studies [3–5]. LH can be done using single-port or multiport techniques. Conventional multiport laparoscopy requires three or more trocars. Single trocar access is used in single-port laparoscopic hysterectomy (SLH). This single-entry site is often the umbilicus, which also called the natural orifice, and no external scarring occurs. SLH has been associated with less abdominal trauma and better cosmetic results [6]. Vaginal hysterectomy is also a natural orifice technique that is used to reach the peritoneal cavity through the vagina. However, it is unclear which natural orifice hysterectomy is associated with less inflammation.

Surgery has been shown to suppress the postoperative inflammatory response [7–9]. Systemic leukocytic alterations, such as leukocytosis, neutrophilia, and lymphopenia, occur in response to operations because of the effects of various hormones and cytokines [10, 11]. The measurement of leukocytic changes, including neutrophil (NLR) and platelet-lymphocyte

(PLR) ratios, could be a useful method for assessing the postoperative inflammatory response. Minimal invasive surgery should cause less immune impairment, as it is associated with less tissue damage than abdominal surgery is [12–14]. However, there is no information in the literature about how these values change in natural orifice hysterectomies. In the present study, we aimed to investigate the value of alterations in WBC, NLR, and PLR in patients with two natural orifice hysterectomies: SLH and VH.

Although NLR and PLR levels as preoperative and postoperative markers have been the subject of many studies, to the best of our knowledge, this study is the first to evaluate their association with SLH and VH.

MATERIAL AND METHOD

Population

This retrospective study was conducted in the obstetrics and gynecology clinic at Derince Training and Research Hospital. Ethics committee ap-

proval was obtained from the ethics committee of the same institution. This study was also registered in Registry of Clinical Trials; registration number: NCT04221308. The presented study is in accordance with the CONSORT statement.

The study group included patients who underwent hysterectomy between 2018 and 2019. Our hospital is a 50-bed tertiary reference center where approximately 3,500 births per year occur, and about 500 gynecological–oncological surgeries are performed annually. The records of patients who underwent SLH and VH were reviewed retrospectively. The preoperative and postoperative in the first 24 hours hematocrit (HCT), hemoglobin (HB), WBC, PLR, and NLR values as well as their demographic characteristics were compared.

In our clinic, the decision to perform a hysterectomy is made by the gynecology council, which meets weekly. The type of surgery is determined according to the clinical condition of the patient, the gynecological examination, and the patient's request. In general, open surgery is preferred in patients having giant fibroids, many previous surgeries, and immobile uteri. Conditions such as dysfunctional uterine bleeding, cervical intraepithelial neoplasms, and uterine descensus indicate the need for LH or VH. In cases where there is no clinical suspicion, oophorectomy is performed according to the patients' wishes. In benign cases, type 1 hysterectomy is preferred.

In SLH, the procedure is performed as follows. Patients undergo standard preparations prior to SLH. The first assistant handles the scope from the patient's right side. The second assistant, who is positioned between the legs of the patient, inserts a uterine manipulator (Rumi System; Cooper Surgical, Trumbull, CT). At the beginning of the surgery, a 1.5 to 2.5 cm vertical incision is made within the umbilicus using the open Hasson approach. After the bottom retractor ring of the wound retractor component of the Octo-Port is inverted (DalimSurgNet, Seoul, Korea), it is inserted through the incision deep in the peritoneum. Carbon dioxide is insufflated through the gas valve of the Octo-Port to maintain intraabdominal pressure at 10 to 12 mm Hg. Through the 10 mm channels of the Octo-Port, a 10 mm, 30° rigid laparoscope is introduced. Rigid laparoscopic instruments are introduced through the 5 mm channels of the Octo-Port. The utero-ovarian ligament or infundibulopelvic ligament, uterine vessels, and uterine ligaments are transected by using the 5 mm LigaSure vessel sealer device (Blunt Tip; Covidien, Dublin, Ireland). Vaginal cuff closure is done using laparoscopic intracorporeal suturing and the knot-tying technique.

In VH, the patients are placed in the dorsolithotomy position. The steps are as follows. A round incision is made in the cervix, the bladder is dissected, the peritoneal cavity is entered anteriorly or posteriorly, the uterine arteries are ligated, the ovarian round ligament or infindibulopelvic ligament is cut, the uterus is removed, and the peritoneum and vaginal cuff are sutured.

In the present study, patients with a chronic disease (e.g., hypertension, diabetes mellitus, and rheumatologic, nephrological, and hematological diseases), the presence of active infection, corticosteroid use, acetylsalicylic acid, and anticoagulant use were not included in the present study. Patients who underwent cystocele or rectocele repair with mesh were not included in the study because of the potential effects on inflammatory outcomes. Bladder and bowel injuries, blood transfusion requirements, wound infection and hematoma, postoperative respiratory system complications (e.g., atelectasis) were evaluated as surgical complications.

Blood tests

Maternal venous blood samples are placed in hemogram tubes with 2–2.5 ml ethylenediaminetetraacetic acid (EDTA) and then homogenized. The calibrations of the device are completed and analyzed using the Pentra DF Nexus Hematology System® (Horiba Healthcare, Japan). PLR and NLR are calculated by dividing the platelet and neutrophil counts, respectively, by the lymphocyte count.

STATISTICAL ANALYSIS

In the present study, the Number Cruncher Statistical System (NCSS, 2007) (Kaysville, UT, USA) software was used in the statistical analysis of the data. Descriptive statistics, such as mean, standard deviation, median, first quartile, third quartile, frequency, and percentages, are shown in the tables 1 and 2. The Shapiro-Wilk test and graphical examinations were conducted to and check the normality assumption. The independent sample t-test and the Mann-Whitney U test were conducted to compare the quantitative variables between the SLH and VH groups. A paired t-test and the Wilcoxon signed-ranks test were conducted to determine the within-effects of the quantitative variables. The qualitative variables were compared by applying the Pearson chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

Hysterectomy was performed in 148 patients, 47 of which used the single-port technique; 101 were performed using the vaginal route. One patient in the first group and 13 patients in the second group did not meet our inclusion criteria. Finally, the data on the 46 patients in the SLH group and the 88 patients in the VH group were evaluated. Oophorectomy had been performed on 16 patients in the SLH group and 23 patients in the VH group. Our study groups consisted of patients who did not have any disease, did not use medication, and underwent hysterectomy for benign reasons.

The demographic features and inflammatory markers are shown in Tables 1 and 2. There were no significant differences in the demographic data between the groups. The most common indication in the VH group was uterine descensus, whereas the most common indication in the SLH group was dysfunctional uterine bleeding. Although no difference in complications was found, the length of hospital stay was lower in the VH group. The durations of

operations were lower in the VH group. Regardless of the procedure, WBC, NLR, and PLR were increased, and HB and HCT were decreased in all groups in the postoperative period. However, the changes in WBC, NLR, and PLR were similar in both groups. Moreover, in the postoperative period, the changes in the inflammatory markers—WBC, NLR, and PLR—were not statistically significant.

Table 1: Evaluation of descriptive characteristics by type of operation.

	SLH (n= 46)	VH (n= 88)	p-value
Age (mean±sd)	48.87±5.79	59.72±8.58	a<0.001**
Gravida (min-max)	2 (2, 4)	3 (2, 4)	b0.004**
BMI (kg/m²) (mean±sd)	23.7±2.1	24.1±2.4	a0.284
Systemic disease (%)	12 (26.1)	33 (37.5)	c0.184
Previous surgery (%)	16 (34.8)	22 (25)	c0.233
Indications (%) dysfunctional uterine bleeding	17 (36.9)	23 (26.1)	c0.213
symptomatic fibroids	12 (26)	15 (17)	c0.523
adnexal mass	10 (21.7)	12 (13.6)	c0.815
desensus uteri	4 (8.6)	30 (34)	c<0.001**
endometrial hyperplasia	2 (4.3)	6 (6.8)	c0.876
cervical intraepithelial hyperplasia	1 (2.1)	2 (2.2)	c0.542
Total operation time (minute) (mean±sd)	45.4 ±20.2	75.2±34.2	a<0.001**
Duration of hospital stay (days) (min-max)	4 (2, 4)	2 (2, 3)	b<0.001**
Complications (%)	3 (6)	4 (4)	b 0.542

*a Independent samples t-test, b Mann-Whitney U test, c Pearson chi-square test, **p<0.01. BMI: body mass index; Max: maximum; Min: minimum; Sd; standard deviation; SLH: single-port laparoscopic hysterectomy; VH: vaginal hysterectomy*

Table 2: Evaluation of WBC, HGB, HCT, and NLR measurements by operation type.

		SLH	VH	p-value
WBC (mean±sd)	Preop	7.34±1.93	6.73±2.18	a0.113
	Postop	11.4±3.55	10.69±2.86	a0.206
	Difference	4.07±3.23	3.96±2.59	a0.832
	dp	<0.001**	<0.001**	
HGB (mean±sd)	Preop	11.74±1.64	12.86±1.31	a<0.001**
	Postop	10.37±1.35	10.74±1.04	a0.109
	Difference	-1.37±0.93	-2.12±1.33	a0.001*
	dp	<0.001**	<0.001**	
HCT (mean±sd)	Preop	35.6±4.36	38.5±3.82	a<0.001**
	Postop	31.55±3.76	32.78±3.26	a0.051
	Difference	-4.05±2.75	-5.73±3.99	a0.012*
	dp	<0.001**	<0.001**	

*a Independent samples t-test, b Mann-Whitney U test, d Paired t-test, e Wilcoxon signed-ranks test, *p<0.05, **p<0.01, HB: hemoglobin; HCT: hematocrit; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; Postop: postoperative value; Preop: preoperative value; Sd: standard deviation; SLH: single-port laparoscopic hysterectomy; VH: vaginal hysterectomy*

DISCUSSION

Wheeless et al. were the first to describe the "scar-free" laparoscopic tubal ligation technique [15]. It is aimed at decreasing postoperative pain and scarring by reducing both the number and size of the trocar. Although SLH provides cosmetic benefits and reduces abdominal trauma, initially, it was not widely performed because of technical difficulties [16]. However, because of advances in technology, the development of multilumens and flexible instruments as well as increasing surgical experience, these methods have become more widely used [17-19]. VH is also a natural orifice technique that is used to reach the abdominal cavity through the vaginal orifice [20]. Both SLH and VH are associated with low morbidity, low minor and major complications in the day case setting [21].

The inflammatory responses in laparoscopy and open surgery have been evaluated in many previous studies [22–24]. The lower tissue trauma in laparoscopic surgery may be associated with the lower response to systemic inflammation [25], which is one of the advantages of laparoscopy [7, 26, 27]. It is therefore reasonable to assume that there is a lower inflammation response in the single-port technique.

NLR and PLR measurements, unlike other immune mediators such as interleukins, are inexpensive and simple tests conducted in routine practice. Although NLR and PLR have been studied in many diseases, such as various cancers, inflammatory diseases, and preeclampsia, they have not been evaluated in SLH. Therefore, it is crucial to demonstrate WBC, NLR, and PLR changes in these patients. We believe that these values are predictors of postoperative morbidity and mortality. In the present study, our findings showed that morbidity was low in both groups, so no difference was found in this respect. It could also be expected that the energy modality used in SLH would affect inflammation. A bipolar electrosurgery modality was used in all patients in both groups.

In our study, the inflammatory markers were increased after surgery, which was expected. However, the changes in inflammatory markers were the same in both natural orifice techniques, which indicates that both surgeries would be appropriate with regard to inflammation. The exchange of HB and HCT was less in SLH. We believe that the use of energy modality and larger magnification in SLH are responsible for reduced bleeding. In our study, the duration of SLH operations was longer. In the SLH group, operation duration, hospitalization duration, and the learning curve of surgeons were higher than in the VH group, which may have depended on experience. We think that the duration of the operation will decrease as surgical experience in performing this technique increases. Furthermore, surgeons and patients should be aware that in up to 3.5% of single-port hysterectomies, an additional port is required [28]. In our study, all SLH operations were successfully completed using a single-port without the need for additional ports. All vaginal cuffs were closed by a singleport laparoscopy.

The advantages of a single-port system include better cosmetic results and reduced trocar insertion-related complications, wound infection, hematoma, hernia, and pain [29, 30]. Caution is urged in interpreting the results of studies on single port hysterectomies because the evidence is lacking in quality. None of the patients in the present study had incisional or port site hernia. In addition, there was no requirement for blood transfusion. In our study, because the number of complications was small, the complication rates could not be compared.

The limitations of our study include its retrospective design. The number of cases was too small to compare morbidity. Another important point is that in the present study, the SLHs were performed by experienced gynecologists, each of whom had more than five years of experience in this surgical procedure. However, the VHs were performed by less experienced gynecologists. This difference in surgical experience could have biased the results of our study. In addition, there was no data on long-term outcomes. However, the strength of this study is that it is the first in the literature to compare the inflammation markers between the two natural orifice techniques, SLH and VH.

There were no differences in the inflammatory markers in either scar-free operation. This result was obtained by inexpensive and straightforward tests used in daily practice. As the surgical experience in performing SLH increases, the durations of operations and hospital stays will decrease. However, because SLH is still an expensive procedure that requires highly technological equipment, VH operations will continue to be implemented in clinical practice.

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