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Comparison of perioperative outcomes for endometrial cancer staging via traditional laparotomy, laparoscopy and robotic-assisted surgery: short term initial experience.

Geleneksel laparotomi, laparoskopi ve robot yardımlı cerrahi ile endometrial kanser evrelemesinin perioperatif sonuçlarının karşılaştırılması: kısa süreli ilk deneyim

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ÖZ

Amaç:Bu çalışmanın amacı, dünyada ve Türkiye'de en sık görülen jinekolojik kanser türü olan endometrium kanseri evrelemesinde geleneksel abdominal histerektomi (TAH), total laparoskopik histerektomi (TLH) ve robotik yardımlı histerektominin (TRH) perioperatif sonuçlarını karşılaştırmaktır.

Gereç ve yöntemler: Çalışmada endometriyal kanser nedeniyle evreleme cerrahisi yapılan 58 hasta dahil edildi. Tüm olgular Şubat 2015-Mayıs 2016 tarihleri arasında aynı jinekolojik onkolog (E.B.) tarafından Sağlık Bilimleri Üniversitesi Adana Numune Eğitim ve Öğretim Hastanesi'nde opere oldu. Primer sonuç ölçütü perioperatif komplikasyonlardı. İkincil sonuç ameliyat süresi, ameliyat sonrası hemoglobin düşüşü, kan transfüzyon oranları ve hastanede kalış süresi idi.

Bulgular:23 olgu laparotomi, 10 olgu laparoskopi ve 25 olgu robotik asiste olmak üzere 3 grup belirlendi. Gruplar arasında yaş, parite, derece ve miyometrial invazyon derinliği açısından istatistiksel olarak anlamlı fark yoktu. Genel komplikasyon oranı TAH grubunda daha yüksekti. TRH ve TLH hastalarında, TAH hastalarına kıyasla böbrek yetmezliği, idrar yolu enfeksiyonu ve ameliyat sonrası ateş görülme olasılığı daha düşüktü. TRH grubundaki hemoglobin düşüşü diğer gruplardan daha azdı fakat istatisiksel olarak anlamlı değildi (p= 0,797). Ortalama ameliyat süresi TRH olgularında TLH ve TAH olgularına göre daha uzundu (sırasıyla 300, 230, 165 dakika). TAH, TLH ve TRH hastalarının ortanca hastanede kalış süreleri sırasıyla 5, 3 ve 2 gündü (p < 0.0001). Minimal invaziv cerrahi gruplarında (TLH'de 0/10 vaka ve TRH'de 3/25 vaka) geleneksel yaklaşımlardan (TAH'da 5/23 vaka) önemli ölçüde daha az kan transfüzyonu gereksinimi vardı.

Sonuçlar: Kısa vadeli ilk deneyimlerimizle, minimal invaziv cerrahi yaklaşım üstün perioperatif sonuçlarla sonuçlandı. Daha uzun ameliyat sürelerine rağmen, bu çalışmadan elde edilen sonuçlar endometriyum kanserinin tedavisinde robot yardımlı cerrahi evrelemenin hem uygulanabilir olduğunu hem de daha kısa hastanede kalış süresi ile ilişkili olduğunu göstermektedir.

Anahtar Kelimeler: Endometriyal kanser; Laparoskopik cerrahi; Robotik cerrahi; Perioperatif komplikasyonlar

ABSTRACT

Aim: To compare the perioperative outcomes of traditional abdominal hysterectomy (TAH), total laparoscopic hysterectomy (TLH), and robotic-assisted hysterectomy (TRH) for endometrial cancer staging, which is the most common gynecological cancer type in Turkey Materials and Methods: All cases were performed by the same gynecologic oncologist (E.B.) from February 2015 to May 2016 in Adana Numune Education and Training Hospital. The study was conducted retrospectively. The primary outcome measure was perioperative complications. The secondary outcome measures were operative time, postoperative hemoglobin drop, blood transfusion rates and length of the hospital stay

Results: 23 cases were laparotomy (TAH), 10 cases were laparoscopy (TLH), and 25 cases were robotic-assisted (TRH) There were no statistically significant differences between the groups in terms of age, parity, grade and depth of myometrial invasion. The overall complication rate was higher in the TAH group.TRH and TLH patients were less likely to have renal failure, urinary tract infection and postoperative fever compared to TAH patients. The decrease in hemoglobin in the TRH group was less than in the other groups, but it was not statistically significant (p= 0.797).Mean operative time was longer in TRH cases than in TLH and TAH cases (300, 230, and 165 minutes, respectively).The median lengths of hospitalization for TAH, TLH, and TRH patients were 5, 3, and 2 days, respectively (p < 0.0001) There were significantly fewer blood transfusion requirements in minimally invasive surgery groups (0/10 case in TLH and 3/25 cases in TRH) than in traditional approaches (5/23 cases in TAH)

Conclusions: With our short term initial experience, minimally invasive surgical approach resulted in superior perioperative outcomes. Despite longer operative times, the results from this study suggest that robotic-assisted surgical staging in the management of endometrial cancer is both feasible and associated with a shorter length of hospitalization.

Keywords: Endometrial cancer; Laparoscopic surgery; Robotic surgery; Perioperative complications

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INTRODUCTION

Endometrial cancer is the second most common gynecologic malignancy worldwide and the most common in Turkey. According to the results of the World Health Organization (WHO) for 2020, endometrial cancer ranks 5th at 5.9% in terms of the number of new cases among women of all ages in Turkey (1). Endometrial cancer is the most commonly diagnosed type of gynecological cancer in Turkey, occurring at a median age of 58 years (2). During this period, the average incidence of uterine cancer was 10.36 per 100,000, or 3851 new cases per year (2).

The way cancers are staged has evolved over the last 70 years to keep pace with the rapid growth of medical research and practice, particularly in oncology (3). According to FIGO (The International Federation of Gynecology and Obstetrics) decisions from 1988, the laparotomy approach is the traditional method for surgically staging endometrial cancer (4, 5). Along with the early diagnosis, proper staging surgery is critical for the disease's prognosis. A total extra-facial hysterectomy, bilateral salpingo-oophorectomy (BSO), and pelvic-paraaortic lymph node dissection (PPLND) are the standard surgical methods for diagnosing and treating endometrial cancer, but there are many other options (6). Additional surgical approaches include vaginal, TLH, or TRH staging. After Reich et al. (7) published TLH hysterectomy cases in 1988, Dargent et al. (8) described TLH lymphadenectomy in gynecological malignancies in 1989. In 1991 and 1993, Querleu et al. (9, 10) published about the first time they did a transperitoneal pelvic lymphadenectomy on 39 people with cervical cancer. Nezhat et al. (11) published the first TLH paraaortic lymphadenectomy in 1992. Today, the widespread use of TLH in many areas has also aided in the advancement of laparoscopy in gynecological oncology (12). Studies and meta-analyses show that the use of TLH in the staging and treatment of endometrial cancer reduces perioperative morbidity, shortens hospital stay, and has similar efficacy, mean survival, and disease-free survival compared to TAH (13). This is because TLH applications have some problems, like limited mobility and poor image quality. TRH was born out of this desire to do the best job possible with the least amount of surgery (14). In Turkey, Göçmen et al. (15) reported in a study published that TRH enables three-dimensional imaging and more comfortable movement, allowing for the endoscopic treatment of more complex cases. Despite these advantages, TRH surgery has several disadvantages, including a lack of tactile sense, long setup time, and high cost.

This study was to compare the perioperative results of patients who underwent TAH, TLH, TRH, and staging surgery with the diagnosis of endometrial cancer in our clinic. This study's aim was to compare the perioperative results of patients who underwent TAH, TLH, TRH, and staging surgery with the diagnosis of endometrial cancer in our clinic. On the other hand, we aimed to determine whether TLH and TRH, as minimally invasive surgical methods, have superiority over each other in terms of perioperative results.

MATERİAL AND METHODS

Our study was planned as a retrospective cross-sectional analysis, and included 23 TAH, 10 TLH, and 25 TRH patients who were operated on for endometrial cancer in the Department of Obstetrics and Gynecology of Health Sciences University Adana Numune Training and Research Hospital between February 2015 and May 2016. The procedures were in accordance with the ethical standards set by the responsible human experimentation committee (institutional and national) and 1975 Helsinki Declaration. The inclusion criteria specified that participants must be between the ages of 18 and 85 and have undergone endometrial cancer surgery. The criterion for exclusion was the presence of synchronous cancers. We received approval for the study from the Ethics Committee of Adana Numune Training and Research Hospital, University of Health Sciences, on June 28, 2016, with decision number 95.

Endometrial biopsy with a Pipelle curette is often sufficient for diagnosis in patients with suspected endometrial cancer. However, false negative rates of Pipelle curette endometrial biopsy are reported to be 10%. For this reason, in symptomatic patients with a strong suspicion of endometrial cancer, we make the diagnosis in our clinic with fractionated dilatation and curettage (16). Transvaginal ultrasonography and chest radiography were found to be sufficient for the initial evaluation of patients with endometrioid type histology. Advanced radiological evaluations (magnetic resonance imaging, computed tomography) were performed in the presence of suspected extrauterine spread (17). Ca-125 and whole-body computed tomography were added to the preoperative evaluation to see if there was a spread outside of the uterus (18).

We staged endometrial cancer according to the 2009 FIGO staging system. Primary treatment included surgical staging, and we planned adjuvant treatment according to the stage of the disease. Total hysterectomy and BSO, which are the recommended approach in grade 1-2 patients with endometrioid type histology preoperatively, were performed. It was decided whether we should send the specimen for frozen pathological evaluation and lymph node dissection should be performed according to the risk factors for extra-uterine spread (19, 20). Due to the increased risk of extrauterine spread in patients with non-endometrioid histology or grade 3 endometrioid histology, a complete staging surgery was performed, including abdominal hysterectomy, BSO, omentectomy, and bilateral PPLND (21). In the case of intra-abdominal spread, cytoreductive surgery procedures like those used for ovarian cancer were thought about, with the goal of leaving no tumor behind (22, 23). At the time of admission, patients who were diagnosed with endometrial cancer because of Lynch syndrome were excluded from the study. One gynecologic oncology surgeon with TRH experience performed all necessary robotic surgeries using the da Vinci® Si HD - Cordamed surgical system. Two gynecological oncology surgeons and one obstetrician and gynecologist performed the TLH and TAH procedures. The surgical technique was decided in collaboration with other gynecological oncology specialists during an oncology council meeting during which each patient was presented prior to surgery. As a result of the meeting, it was determined that the patient was not a candidate for minimally invasive surgery, and the same surgical team performed the open procedure (24).

Age, number of children, type of endometrial cancer, type of surgery performed, grade and stage of the tumor, number of pelvic-paraaortic lymph nodes, duration of operation, adverse events, length of hospital stay, and complete blood count chan-

ge (preoperative compared to postoperative hemoglobin) were all collected. The operative time was calculated as the time from the surgeon initiating the skin incision to the wound line being closed. The time spent in the theatre was tracked from the time the patient entered to the time they exited. All patients met the same discharge criteria: they restored their mobility without help, tolerated a restricted diet, and maintained pain control with oral medications.

Statistical analysis

The IBM SPSS for Windows V24.0 package program was used to analyze the data. The Shapiro-Wilk test was used to determine whether the variables were suited for normal distribution. The mean and standard deviation were used to highlight variables that met the assumption of normal distribution, while the median (minimum–maximum) was used to summarize variables that did not meet the assumption. Numbers and percentages were used to summarize categorical variables. The cross tables were analyzed using the chi-square test. When the normal distribution condition was not met in group comparisons, the Kruskal-Wallis test was used to detect the difference between more than two groups, and Dunn's test was used to discover which groups contributed to the difference. In the case where the assumption was provided, the ANOVA test was used. The statistical significance level of $p < 0.05$ was accepted.

RESULTS

As shown in Table 1, there is no significant difference in mean age among the TAH, TLH, and TRH groups (p=0.57).

Table 1. Age and parity characteristics of the groups.

	TAH (n=23)	TLH (n=10)	TRH (n=25)	p value
Age	60.6 ± 11.6	62.6 ± 9.5	58.4 ± 10.8	0.57
Parity	3 (2 – 5)	3 (0 – 4)	3 (2 – 4)	0.59

The statistical analysis was performed with Chi-Square analysis

As shown in Table 2, there is no significant relationship between the grade and the groups (p=0.270) and the degree of myometrial invasion and the groups (p=0.738)., there is a significant difference between the groups in terms of the number of pelvic lymph nodes (p<0.001). The TAH group differed significantly from the other groups in terms of the number of paraaortic lymph nodes and total lymph nodes count (p<0.05 and p<0.001, respectively) in

Table 2. Distribution of the groups by the grade, the degree of myometrial invasion and the number of lymph nodes

	TAH	TLH	TRH	p value
Grade1 (n, %)	12 (54.5%)	3 (30%)	13 (52%)	0.270
Grade2 (n, %)	7 (31.8%)	7 (70%)	8 (32%)	
Grade3 (n, %)	4 (13.6%)	-	4 (16%)	
Myometrial invasion depth less than 50%	13 (56%)	7 (70%)	16 (64%)	0.738
Myometrial invasion depth more than 50%	10 (43%)	3 (30%)	9 (36%)	
Total Lymph Nodes Count (min.-max.)	42 (11 – 66) *	20 (6 – 43)	21.5 (13 – 38)	**< 0.001**
Paraaortic Lymph Nodes Count (min.-max.)	11(3 – 22)	4 (0 – 23)	5 (3 – 8)	**0.005**

The statistical analysis was performed with Chi-Square analysis. *Dunn's test was applied to determine the group that made the difference

As shown in Table 3, the operative times are the longest in the TLH group and the shortest in the TAH group (p<0.001). The length of hospital stay was the shortest in the TRH group and the longest in the TAH group (p<0.001).

Table 3. The distribution of the groups in terms of operation time, hospital stay, and hemoglobin amount decreases.

	TAH (n=23) median (min.–max.)	TRH (n=25) median (min.–max.)	TLH (n=10) median (min.–max.)	p value
Operation time (min.)	165 (110 – 335)*	230 (150 – 390) *	300 (240 – 380) *	< 0.001
Length of hospital stay (days)	5 (3 – 8)*	2 (2 – 4)	3 (3 – 4)	< 0.001
hemoglobin change (g/dl)	1.2 (0.40 – 3.20)	1.1 (0.30 – 3.30)	1.6 (0.70 – 2.0)	0.797

The statistical analysis was performed with one-way ANOVA *Dunn's test was applied to determine the group that made the difference

As shown in Table 4, considering all groups, 55.2% of the patients who are operated on in our clinic were considered to be in stage IA, while 24.1% are considered to be in stage IB.

Table 4. Distribution of groups according to stages..

	TAH (n= 23) (n, %)	TRH (n=25) (n, %)	TLH (n=10) (n, %)	Total (n, %)
IA	11 (47)	14 (56)	7(70)	32 (55.2)
IB	5 (21)	6 (24)	3 (30)	14 (24.1)
II	3(13)	2 (8)	-	5 (8.6)
IIIA	3 (13)	-	-	3 (5.1)
IIIB	-	1 (4)	-	1 (1.7)
IIIC2	1 (7)	2 (8)	-	3 (5.1)

The statistical analysis was performed with Chi-Square analysis

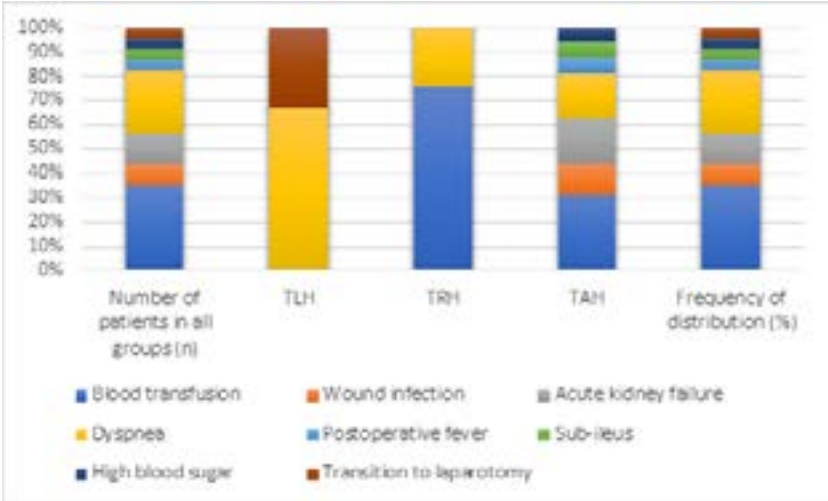
Table 5 and Figure 1 show that complications are frequently seen in the TAH group.PPLND performed in patients in the TAH group increases the risk of bleeding since itis a more invasive surgical intervention than minimally invasive surgical techniques. The large surgical incision area in the TAH group, it brings with it an increase in thenumber of postoperative wound infections. The frequency of acute kidney injury,increased need for blood transfusion, and dyspnea is more common in patients whounderwent TAH, as expected.

Table 5. Complication distributions in all groups

Patients with complications	Number of patients in all groups (%)	TLH (%)	TRH (%)	TAH (%)
No complication	35 (60,3)	-	-	-
Blood transfusion	8(13,8)	-	3 (5.1)	5 (8.6)
Wound infection	2 (3,4)	-	-	2 (3.4)
Acute kidney failure	3 (5,2)	-	-	3 (5.1)
Dyspnea	6 (10,3)	2 (3.4)	1(1,7)	3 (5.1)
Postoperative fever	1(1,7)	-	-	1 (1,7)
Sub-ileus	1 (1,7)	-	-	1 (1,7)
High blood sugar	1 (1,7)	-	-	1 (1,7)
Transition to laparotomy	1(1,7)	1 (1,7)	-	-

The statistical analysis was performed with one-way ANOVA

Figure 1. Complication distributions in all groups



Traditional abdominal hysterectomy (TAH), Total laparoscopic hysterectomy (TLH), and Roboti-c-assisted hysterectomy (TRH)

DISCUSSION

In our study, three available surgical methods were examined in terms of their perioperative results. Since including TRH into the practice of gynecological oncology, the patient group that benefits most from this technology is patients with endometrial cancer. Along with overcoming many of the limitations of traditional TLH, TRH has elevated minimally invasive approaches in gynecological oncology to a new level (25). We know that since most of these patients are obese; they are more prone to complications caused by traditional TAH approaches. Obesity is not only a known risk factor for endometrial cancer, but it also has a big impact on the surgery that is chosen (26). According to the authors, in a study that included obese and morbidly obese endometrial cancer patients and compared TRH and TLH staging, TRH was performed with a shorter operation time, decreased blood loss, increased total lymph node count, and shorter hospital stay in both obese and morbidly obese patient groups (27).

Although TLH staging of endometrial cancer results in less blood loss and faster recovery times, staging has limitations. A longer learning curve for the surgeon, a longer operation time than the TAH approach, and the surgeon's inability to perform complex surgery are some drawbacks of this method (28). According to studies, the learning curve for laparoscopic endometrial cancer surgery is between 20 and 100 cases, allowing the surgeon to achieve a stable operation time and enough lymph node excisions (25). Also, it has been shown that different TLH techniques influence the rates of morbidity and recurrence of tumoral tissue in the vaginal cuff (25).

The da Vinci® Si HD System has many advantages over conventional laparoscopy. Among these are the short learning curve, the 3-dimensional vision it provides in the

surgical field, the articulation of the instruments used, and the surgeon's movement

without force can be considered (29). When we look at the publications comparing the TRH approach and the TAH approach in endometrial cancer surgery, although TRH has longer operation times, it is seen that it has advantages such as less blood loss, reduced transfusion needs, a decrease in complication rates, and shorter hospital stays (30). When compared in terms of lymph node numbers, it was seen that TRH with a laparoscopic approach had similar lymph numbers (31). Due to the shorter learning curve of TRH compared to laparoscopic endometrial cancer surgery, it has found a chance to be widely used in a short time. When compared with both TAH and TLH staging, it has been shown that TRH staging surgery causes less morbidity, especially in the obese patient group (32).

The median age at diagnosis of endometrial cancer is 60 years in the USA (33). In our study, the mean age at diagnosis was 60 in the TAH group, 58 in the TLH group, and 62 in the TRH group. There was no significant difference in age values between the groups ($p = 0.570$). According to the hemogram results on the postoperative first day, the mean decrease in hemoglobin was 1.6 g/dl in the TLH group, 1.2 g/dl in the TAH group, and 1.1 g/dl in the TRH group. TRH patients lost less blood than all other groups. This is in line with the existing literature. In the TLH group, blood loss can be attributed to a surgeon learning curve, fewer patients in that group, and fewer high-resolution images in laparoscopic surgery than in TRH.

In our study, there is a significant difference between the groups in terms of operation time values ($p < 0.001$). Considering that the preparation period was included in the operation times in the TRH group, we observed that the operation time was much shorter compared to the TLH group. Considering that the mean age of patients with endometrial cancer is 60, we would like to point out that there is a shorter staging time in TRH than in TLH due to the accompanying problems in etiology and obesity. In the TRH group, the patient stays in the Trendelenburg position for less time and anesthesia-related complications are less common.

In our study, we found that there was a big difference in the number of totals, pelvic, and paraaortic lymph nodes between the groups ($p<0.001$, $p<0.001$, and $p=0.05$, respectively). While the median total lymph count was 42 in the TAH group, it was calculated as 21.5 in the TLH group and 20 in the TRH. It is well known that the most important oncological parameter in staging surgery is the total lymph count (32). Depending on the learning curve of the surgeon in TRH and TLH operations, there are studies in the literature (34) in which the total number of lymph nodes in TRH is high. The learning curve of the surgeon, different evaluations among pathologists, and the earlier stage of endoscopic patient groups compared to the TAH group can be counted among the reasons for the low number of total lymph nodes in the patient group we performed minimally invasive surgery (35).

In our study, no complications were observed in 60.1% of the patients. Among all groups, 2/3 of the existing complications were observed in the TAH staging group. Our findings were compatible with studies in the literature (32). Three patients in our TAH group were followed up because of impaired renal function tests after surgery. Since wound infection developed in 2 patients in our TAH group, they were hospitalized again after discharge. Due to the development of ileus in 1 patient in the TAH group, postoperative follow-up was performed. The need for blood transfusion was observed at a rate of 5.4% in all patients. Of the eight patients who needed blood transfusions, five were in the TAH group and three were in the TRH group. It was found that none of the patients in the TLH group needed transfusions, and the highest blood transfusion was used in the TAH group, which is consistent with the current literature (32). While an equal number of patients were observed in the TAH and TRH groups due to postoperative dyspnea, dyspnea was observed in only 1 patient in the TLH group. We believe the low number of patients, as well as the advantages of minimally invasive surgery, are among the reasons for the low complication rates in the laparoscopy group. There is a significant difference between the groups in terms of hospitalization duration values ($p<0.001$). While the longest hospitalization period was observed in the TAH group, the shortest hospitalization period in the TRH group is consistent with the current literature (25).

Limitations:

The study's limitations include the fact that it was conducted in a single center and with a relatively small sample size. Additionally, the limited sample size impairs the statistical analysis and limits the generalizability of the findings. Future studies should also include long-term follow-up to find out how long patients live and how they feel about their lives. Our study could not be extended to a long period in the TRH group due to the high costs and the intensity in the hospital operating room.

CONCLUSION

TRH is an advantageous method in gynecological oncology with its high 3D image quality, the quality of surgical equipment brought by minimally invasive surgery, patient satisfaction with pain, and lower postoperative complications compared to TAH. Considering the postoperative complications, patient safety, need for blood transfusion and length of stay in hospital, minimally invasive surgery and especially TRH will find more place in endometrial cancer surgery in the future. More prospective studies are needed on the results of TRH in endometrial cancer surgery.

Conflict of Interest:

The authors declared no conflict of interest.

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