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Evaluation of quality of life and cost-effectiveness of definitive surgery and the levonorgestrel intrauterine system as treatment options for heavy menstrual bleeding

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Background/aim: This study aimed to compare the levonorgestrel intrauterine system (LNG-IUS) with abdominal hysterectomy (TAH) and total laparoscopic hysterectomy (TLH) as first-line treatments for heavy menstrual bleeding (HMB).

Materials and methods: Ninety-eight patients aged 20–55 years who complained of regular heavy menstrual bleeding were enrolled in the study. The TAH group included 29 patients, the LNG-IUS group included 34, and the TLH group included 35. These groups were compared in terms of quality of life and the cost-effectiveness of the selected methods. Quality of life was assessed using the 36-Item Short Form (SF-36), and cost-effectiveness was assessed according to the current cost of each approach.

Results: The quality of life parameters, with the exception of mental health, improved significantly in the LNG-IUS, TAH, and TLH groups. The mean costs of the LNG-IUS, TAH, and TLH procedures were \$99.15 ± 4.90, \$538.82 ± 193.00 and \$1617.05 ± 258.44, respectively (P < 0.05). Overall, LNG-IUS was the most cost-effective treatment option.

Conclusion: The outcome measures of the SF-36 revealed that after 6 months, these treatments were equal in terms of quality of life, except for mental health. LNG-IUS was the most cost-effective approach.

Key words: Cost analysis, levonorgestrel-releasing intrauterine system, menorrhagia, surgery, quality of life

1. Introduction

Heavy menstrual bleeding (HMB) is a widespread gynecological problem that accounts for more than 10% of outpatient referrals to gynecological outpatient clinics (1). HMB can be defined as blood loss that exceeds 80 mL per menstrual cycle (2). HMB may result in sexual dysfunction and psychological morbidity that further affects quality of life and working capacity (3). Although hysterectomy is the last, but definitive, treatment option for HMB, its associated morbidity and complication rate exceed those of other treatment modalities (4), and the high cost of a surgical procedure should always be considered. The levonorgestrel intrauterine system (LNG-IUS) is an effective treatment for HMB (5). Women using the LNG-IUS may stay in the hospital for shorter times and typically are less affected in terms of working capacity. The LNG-IUS is a cost-effective alternative to hysterectomy for the treatment of this disorder (6). The aim of this study is to evaluate the quality of life and cost-effectiveness of

the LNG-IUS compared to total abdominal hysterectomy (TAH) and total laparoscopic hysterectomy (TLH).

2. Materials and methods

The study was performed at the Department of Obstetrics and Gynecology, Adana Numune Education and Research Hospital, Adana, Turkey. A total of 104 patients aged 20–55 years, with complaints of regular HMB, were enrolled in the study from January 2013 to June 2015. Ninety-eight women completed the study. The inclusion criteria were the presence of HMB, reproductive age, a completed family, failure of appropriate first-line oral medical therapy, normal Pap smear, no pelvic pathology on ultrasound, normal endometrial biopsy, and pictorial blood loss assessment chart scores of ≥100 (average of two consecutive cycles). The exclusion criteria were previous endometrial resection/ablation, any uterine pathology on scans or hysteroscopy, incompletely investigated abnormal uterine bleeding, and postmenopausal bleeding. The local ethics committee approved this study.

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A total of 104 women with HMB, who were unresponsive to medical treatment, were informed about their treatment options. Three treatment options were offered to these patients: TAH, TLH, and LNG-IUS. The patients were assigned to three groups according to their treatment choices. The first group consisted of 32 patients who received TAH treatment, the second group included 37 patients who were treated with TLH, and the third group included 35 patients treated with the LNG-IUS. Written informed consent was obtained from each patient. Three patients in the TAH group, one patient in the LNG-IUS group, and two patients in the TLH group were lost to follow-up (Figure 1). All procedures were performed using the same techniques by the same surgeons. Standard preoperative assessments were performed together with pelvic and abdominal examinations, abdominal and transvaginal ultrasound examinations, Pap smears,

and endometrial biopsies to exclude any pathologies. Intraoperative prophylactic antibiotic therapy with cefazolin was administered to the TAH and TLH groups. The patients were discharged from the hospital when they could tolerate a normal diet, were able to dress themselves, and were fully mobile.

The LNG-IUS (Mirena, Schering Oy, Finland) was inserted into the uterine cavity within 7 days of the onset of menstruation. It was loaded into the insertion tube, and after the operator had secured the threads, set the flange, and released the arms, the device was advanced into the uterine fundus and was released, followed by the withdrawal of the inserter.

For the TLH surgeries, the patients were appropriately placed in the lithotomy position. The uterine manipulator was placed before the surgical intervention. An intraumbilical incision was used to induce

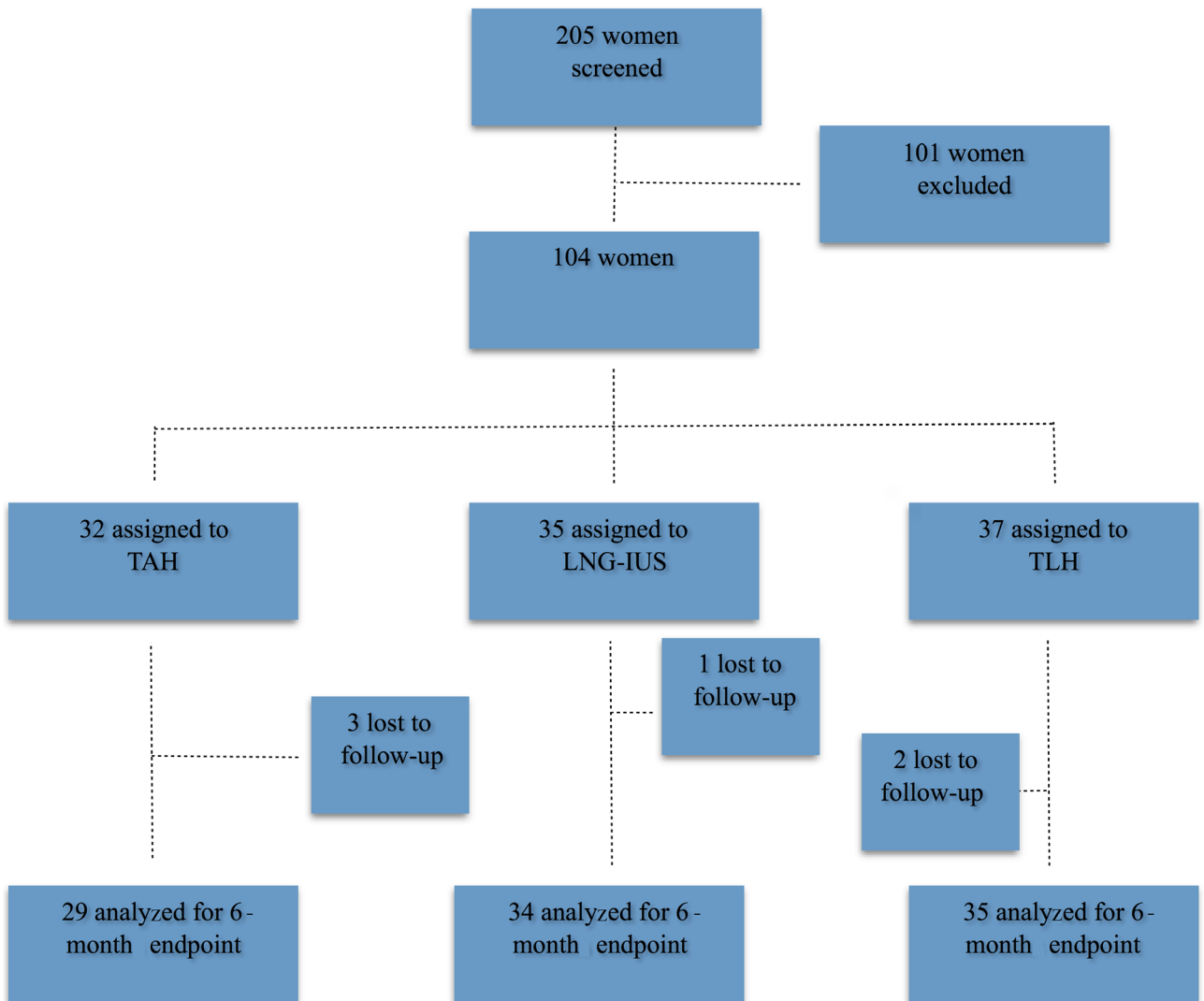


Figure 1. Study design.

pneumoperitoneum. A trocar of 10–12 mm was placed at the umbilicus. Two additional 5-mm satellite trocars were placed in each ilioinguinal area, and a third satellite trocar was placed in the left-upper quadrant as necessary. The uteroovarian and round ligaments were sealed using bipolar electrosurgery. Next, a bladder flap was created. After the bladder flap had been created in the anterior region, the uterine arteries were sealed and cut at the sides at the internal cervical os level. Anterior and posterior culdotomies were performed using monopolar cautery. The uterus was removed and the vaginal cuff was closed.

For the TAH surgeries, following a transverse incision, the peritoneal cavity was entered. The uteroovarian and round ligaments were clamped, cut, and ligated bilaterally. The perivesical space was dissected to separate the bladder. Sharp dissection was used to skeletonize the uterine vessels, which were clamped, cut, and ligated bilaterally. The cervicovaginal junction at the level of the external cervical os was palpated, and an incision was made to enter the vaginal apex. A circumferential vaginal incision was made to amputate the cervix and uterus. The vaginal cuff was closed.

The primary outcome of the trial consisted of a comparison of the patients' quality of life prior to the treatment and 6 months after the completion of the three treatment procedures. Quality of life was measured with the 36-Item Short Form (SF-36). The SF-36 is a 36-item, self-administered questionnaire that yields scores for the following eight domains of life: physical functioning, role limitations-physical, role limitations-emotional, bodily pain, general health perceptions, vitality, social functioning, and mental health. Each of the domains is scored on a 100-point scale on which higher scores indicate better functioning.

The secondary outcome of the trial consisted of the comparison of the cost-effectiveness of each of the three treatment procedures. The costs, including the use of hospital services (i.e. operations, inpatient days, procedures, and outpatient visits) and medication, were obtained from the medical records.

2.1. Statistical analysis

The statistical analyses were performed using SPSS 13.0 for Windows. Descriptive statistics were calculated for all variables. The data are reported as mean \pm SD or median (minimum and maximum), as appropriate. To compare the means between the two groups for normally distributed data, t-tests and paired t-tests were performed. One-way ANOVA was performed to compare the means among the three groups for normally distributed data. $P < 0.05$ was accepted as the prespecified level of statistical significance.

3. Results

This study included 98 women between 20 and 55 years of age. During the study, 34 women were treated with the LNG-IUS, 29 women were treated with TAH, and 35 women were treated with TLH for HMB. In the three groups, all patients completed the 6-month follow-up. The sociodemographic and obstetric characteristics of the women in the study are illustrated in Table 1. The mean ages of the women in the LNG-IUS, TAH, and TLH groups were 41.32 ± 5.76 , 48.37 ± 4.42 , and 45.55 ± 5.20 years, respectively. The mean body mass indices (BMIs) in the LNG-IUS, TAH, and TLH groups were 27.43 ± 4.67 , 30.47 ± 5.23 , and 31.21 ± 4.38 , respectively. The mean parities of the women in the LNG-IUS, TAH, and TLH groups were 2.85 ± 1.50 , 3.82 ± 1.96 , and 3.94 ± 1.82 , respectively. There were significant differences in the sociodemographic and obstetric characteristics among the three groups. These differences were due to the LNG-IUS group. A comparison

Table 1. Sociodemographic and obstetric characteristics of the patients.

	TAH Group 1	TLH Group 2	LNG-IUS* Group 3	P
Age	48.37 ± 4.42	45.55 ± 5.20	41.32 ± 5.76	0.000
BMI	30.47 ± 5.23	31.21 ± 4.38	27.43 ± 4.67	0.003
Parity	3.82 ± 1.96	3.94 ± 1.82	2.85 ± 1.50	0.004
Educational background				0.001
Illiterate	11 (47.8%)	9 (39.1%)	3 (13%)	
Grade school	15 (25.5%)	23 (41.8%)	18 (32.7%)	
High school	4 (30.8%)	2 (15.4%)	7 (53.8%)	
University	0 (0.0%)	1 (14.3%)	6 (85.7%)	

*Statistically significant P-values were found to be caused by the LNG-IUS group following an analysis of the results by Bonferroni post hoc test.

of the educational backgrounds of the three groups is displayed in Table 1. There was a significant difference in educational backgrounds among the three groups ($P = 0.001$).

The SF-36 scores in each of the three groups indicated favorable developments (Table 2). Compared to the baseline values, the 6-month follow-up results indicated improvements in the general health, physical function, physical role, emotional role, social function, vitality, and pain parameters in all three groups. There were significant improvements in these parameters in the three groups. However, significantly greater improvements were observed in the parameters of physical function, physical

role, and emotional role in all groups; general health in the TAH and TLH groups; and social function and vitality in the TLH and LNG-IUS groups ($P < 0.05$). Only the mental health parameters failed to exhibit significant improvements in any group at 6 months ($P > 0.05$).

In the present study, no complications were observed after the TAH or TLH surgeries. One uterine perforation was observed in the LNG-IUS group, and the device was removed laparoscopically. One woman did not benefit from the LNG-IUS after 6 months of follow-up and eventually underwent a hysterectomy.

The analysis of the cost-effectiveness of the treatments is displayed in Figure 2. The mean costs of the LNG-IUS,

Table 2. Quality of life assessments based on the SF-36 measures.

	TAH Group 1			TLH Group 2			LNG-IUS Group 3		
	Preop	Postop	P	Preop	Postop	P	Preop	Postop	P
General health	41.55 ± 15.92	55.17 ± 16.00	0.000	46.42 ± 16.91	58.28 ± 15.76	0.000	53.38 ± 24.51	62.05 ± 20.04	0.030
Physical function	53.44 ± 25.25	77.41 ± 20.38	0.000	49.57 ± 21.53	79.85 ± 15.69	0.000	51.61 ± 31.37	86.47 ± 15.78	0.000
Physical role	21.55 ± 33.88	67.24 ± 34.78	0.000	16.42 ± 27.07	75.00 ± 30.31	0.000	27.20 ± 40.06	77.94 ± 32.42	0.000
Emotional role	27.58 ± 38.90	67.81 ± 30.18	0.000	18.09 ± 28.40	75.23 ± 32.68	0.000	40.19 ± 46.98	73.52 ± 38.29	0.000
Mental health	54.20 ± 20.18	60.13 ± 13.33	0.213	55.76 ± 15.34	56.58 ± 13.47	0.816	63.29 ± 19.03	66.23 ± 14.81	0.374
Social function	57.76 ± 28.62	67.67 ± 22.29	0.078	42.50 ± 28.63	73.57 ± 16.82	0.000	50.00 ± 23.64	72.43 ± 19.41	0.000
Vitality	41.03 ± 20.15	52.93 ± 16.77	0.035	34.14 ± 19.57	53.57 ± 17.88	0.000	46.17 ± 19.34	64.41 ± 13.96	0.000
Pain	45.34 ± 25.23	67.67 ± 22.29	0.000	48.78 ± 26.81	73.57 ± 16.81	0.001	55.66 ± 29.15	72.42 ± 19.40	0.003

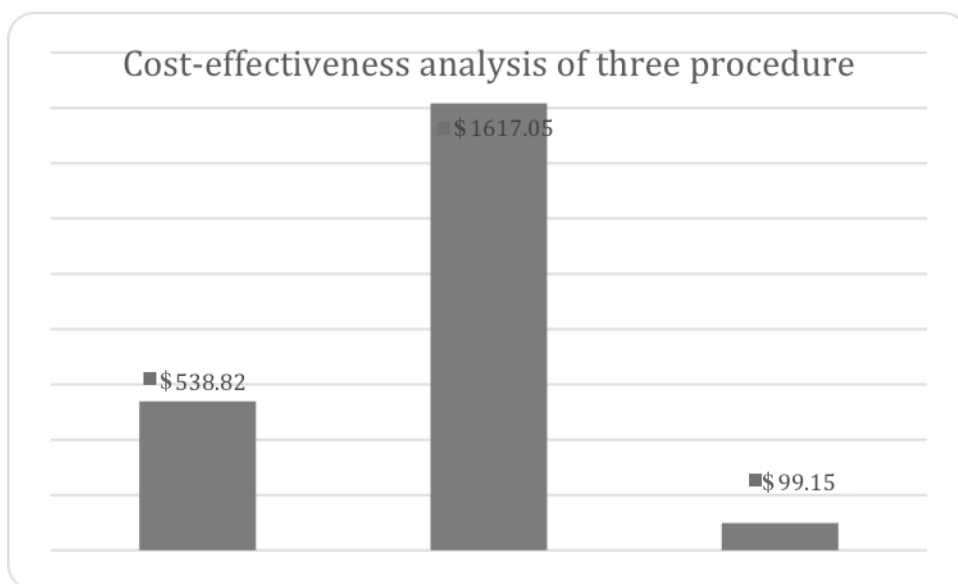


Figure 2. Cost-effectiveness analysis of three procedures.

TAH, and TLH groups were $\$99.15 \pm 4.90$, $\$538.82 \pm 193.00$, and $\$1617.05 \pm 258.44$, respectively. The LNG-IUS was the most cost-effective treatment choice. All costs were significantly lower in the LNG-IUS group than in the TAH and TLH groups ($P < 0.05$).

4. Discussion

HMB is a common gynecological problem that significantly impairs the quality of life of many women. A variety of medical and surgical therapies have been proposed for HMB. Hysterectomy for HMB is most effective in reducing menstrual bleeding and improving the quality of life for most women (7), but this procedure is associated with several complications (6). Following surgery, patients must stay in hospital, and returning to daily and working life takes a long time. However, the LNG-IUS is usually inserted in outpatient gynecology clinics and does not affect patients' daily or working lives. Additionally, the LNG-IUS successfully decreases menstrual blood loss in most women (6,8). Kingman et al.'s study revealed that the LNG-IUS can reduce menorrhagia in women with inherited bleeding disorders (9).

HMB is a commonly encountered gynecological problem in perimenopausal women. Menopause transition includes a period of about 4–5 years before menopause, or sometimes only several months, characterized by varying degrees of somatic and psychological changes that reflect the change in the ovarian cycle (10). Irregularity of the menstrual cycle marks the start of the menopausal transition in most women. Usually around their mid-forties, women's cycle length may initially shorten and then progressively lengthen with the approach of the final menstrual period (11). This irregularity seems to correspond to changes in estrogen levels, which are predominantly the consequence of a decline in ovarian follicle numbers (12). The treatment for HMB in menopause transition is either hormonal or surgical, depending on the patient's symptoms and diagnosis (13).

HMB is a common complaint and causes physical, mental, and emotional problems for many women. In the literature, the treatment of menorrhagia has been shown to improve the quality of life (14–16). The results of our study clearly demonstrated that all treatments (i.e. TAH, TLH, and LNG-IUS) reduced HMB and improved

the women's quality of life at the 6-month follow-up. Significant improvements were observed in the general health, physical function, physical role, emotional role, social function, vitality, and pain parameters in all groups, but no improvements were noted in the mental health parameters in any group.

The follow-up time was only 6 months. TLH is less invasive and traumatic than the abdominal approach (17), but it is a more expensive treatment than TAH. Although the treatment effect is enduring, most complications occur after surgery. In our study, the LNG-IUS was much more cost-effective than TLH and TAH at the 6-month follow-up, but this system may cause unexpected costs during longer follow-ups. Therefore, long-term evaluations of our study groups are necessary. Bleeding and spotting disorders associated with the LNG-IUS are common during the first few months and in most cases are resolved after 3–6 months of use (18). In the literature, the reported removal rate of the LNG-IUS due to bleeding problems is low (19,20). In the present study, bleeding problems that led to the removal of the IUS and subsequent hysterectomy were observed in one woman. Uterine perforation is one of the most serious complications associated with the LNG-IUS, and although this complication is rare, its frequency is likely to increase due to the increasing popularity of the LNG-IUS (21). Laparoscopic surgical removal of an intraperitoneal LNG-IUS is a safe and preferred method (22). In our study, one uterine perforation was observed, and the device was removed laparoscopically.

Cost-effectiveness analysis is an important component of clinical trials (23,24). HMB is a major health problem for women and requires different treatments. Hence, health spending for HMB varies with the treatment options. It is important to select the most cost-effective HMB treatment approach.

In a review article, the LNG-IUS was found to be a cost-effective option for the treatment of HMB, and it provided benefits that were at least similar to those of surgical procedures in terms of health-related quality-of-life outcomes (25). In our trial, the outcome measures of the SF-36 revealed that after 6 months these treatments were equal in terms of quality of life with the exception of mental health, but the LNG-IUS was the most cost-effective approach.

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