

## Comparison of The Outcomes of ART Treatment Between Patients < 36 And ≥ 36 Years of Age with Low Serum AMH Levels

Serum anti-Müllerian Hormon (AMH) Düzeyleri Düşük Olan < 36 ve ≥ 36 Yaş Hastaların YÜT Sonuçlarının Karşılaştırılması

Selçuk SELÇUK<sup>1</sup>, Çetin KILIÇÇI<sup>1</sup>, Bülent Emre BİLGİÇ<sup>2</sup>, Mehmet KÜÇÜKBAŞ<sup>1</sup>, Melda KUYUCU<sup>1</sup>, Hüseyin Tayfun KUTLU<sup>1</sup>

1. Dr. Zeynep Kamil EAH, Jinekoloji Bölümü. İstanbul, Turkey

2. Dr. Zeynep Kamil EAH, Embryoloji Bölümü, İstanbul, Turkey

### ABSTRACT

**Objective:** To compare the outcomes of ART treatment between women < 36 years and ≥ 36 years of age with low serum AMH levels.

**Material and Method:** Patients who underwent intracytoplasmic sperm injection (ICSI) treatment with low AMH levels at our infertility clinic were enrolled into the study, retrospectively. Patients were divided into two groups as < 36 years and ≥ 36 years of age. The outcomes of ART treatment were compared between two groups.

**Results:** The total numbers of embryos were found significantly higher in women < 36 years of age than in women ≥ 36 years of age with low AMH levels. The total number of top quality embryos on day 1 was lower in women ≥ 36 years of age than in women < 36 years of age and the difference between two groups showed statistically significance. The biochemical, clinical, and ongoing pregnancy rates of women < 36 years of age were higher than women ≥ 36 years of age; however only the ongoing pregnancy rate showed statistical significant difference. The cycle cancellation rates of women < 36 years and women ≥ 36 years of age were 1.7% and 15.2%, respectively and the difference was found as statistically significant.

**Conclusion:** The higher ongoing pregnancy rates and embryo quality in younger women is an important outcome to encourage the young women with low serum AMH levels for ART treatment option. Age should take into account in the management and information of women with low AMH level in terms of pregnancy rates and characteristics of ART treatment particularly cycle cancellation rates.

**Keywords:** assisted reproduction techniques; anti-müllerian hormone; age

### ÖZET

**Amaç:** Serum anti-Müllerian hormon (AMH) düzeyleri düşük olan ve yardımcı üreme teknikleri (YÜT) ile tedavi edilen < 36 yaş ve ≥ 36 yaş hastaların sonuçlarının karşılaştırılması.

**Gereç ve Yöntem:** Bu çalışmada, kliniğimizde serum AMH düzeyleri düşük olan ve intrasitoplazmik sperm enjeksiyon tedavisi uygulanan hastalar çalışmaya dahil edildi. Hastalar < 36 yaş ve ≥ 36 yaş olmak üzere iki gruba ayrıldı. YÜT tedavi sonuçları iki grup arasında karşılaştırıldı.

**Bulgular:** Total embryo sayısının; < 36 yaş hasta grubunda ≥ 36 yaş hasta grubuna göre istatistiksel olarak daha yüksek olduğu saptandı. 1.gün top quality embryo sayısı, ≥ 36 yaş hasta grubunda < 36 yaş hasta grubuna göre anlamlı olarak daha düşük bulundu. Biyokimyasal, klinik ve devam eden gebelik oranları < 36 yaş hasta grubunda, ≥ 36 yaş hasta grubuna göre daha yüksekti ancak sadece devam eden gebelik oranı iki grup arasında anlamlı farklılık gösterdi. Siklus iptal oranı; < 36 yaş hasta grubunda %1.7 iken ≥ 36 yaş hasta grubunda %15.2 olarak tespit edildi ve iki grup arasındaki fark istatistiksel olarak anlamlı bulundu.

**Sonuç:** Serum AMH düzeyi düşük olan genç hasta grubunda devam eden gebelik oranı ve embryo kalitesinin daha yüksek bulunması; bu hasta grubunun YÜT tedavisine yönlendirilmelerini desteklemektedir. Yaş, serum AMH düzeyi düşük olan hastaların bilgilendirilmesinde ve yönetiminde YÜT tedavi sonuçları ve özellikle siklus iptal oranları açısından dikkate alınmalıdır.

**Anahtar Kelimeler:** yardımcı üreme teknikleri; anti-müllerian hormon; yaş

### Contact:

**Corresponding Author:** Selçuk SELÇUK

**Address:** Zeynep Kamil Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi, Uskudar, İstanbul, Turkey

**Tel:** +90 (216) 391 06 80

**E-mail:** md\_sel@hotmail.com

**Submitted:** 28.01.2016

**Accepted:** 22.02.2016

**DOI:** <http://dx.doi.org/10.16948/zktb.81170>

## INTRODUCTION

The most reliable and accurate marker of ovarian reserve is considered as anti-Müllerian hormone (AMH) (1, 2). The various studies reported that the AMH was superior to other described ovarian tests such as age, antral follicle count (AFC), basal levels of estradiol (E2), follicle stimulating hormone (FSH), luteinizing hormone (LH), inhibin B (2, 3). AMH is accepted as the best marker for the prediction of the ovarian response to gonadotropins in assisted reproductive technology (ART) (2, 4-6). The ovarian response to controlled ovarian stimulation with gonadotropins is essential for the outcomes of ART cycles (7).

The serum AMH level of less than 0.5–1.1 ng/ml is defined as an abnormal ovarian reserve test result and the low levels of the AMH predict the poor response to ovarian stimulation of in vitro fertilization (IVF) treatment. The poor ovarian response to gonadotropin stimulation could cause to higher rate of cycle cancellation, decline in the fertilization rate and chance of the pregnancy after ART treatment (8). The lower numbers of retrieved oocytes, fertilization and implantation rates, decline in oocyte and embryo quality and increasing in the abortion rate were the major negative factors of aging on outcomes of IVF treatment (9). The different studies reported that the rate of oocyte aneuploidy was higher among older women. The rate of oocyte aneuploidy was found as 10% in women < 35 years, 30% at the 40 years and 100% in women > 45 years (10). The pregnancy rates after IVF treatment decreased with aging and the various studies stated the cutoff age as 36 years old for the beginning of the significant decline in pregnancy rates (11-13).

The outcomes of ART treatment of young women with low serum AMH levels may show differences from older women because of the abovementioned negative factors of aging on outcomes of ART treatment.

Therefore; we aimed to compare the outcomes of ART treatment between women < 36 years and  $\geq$  36 years of age with low serum AMH levels.

## MATERIAL AND METHOD

In present retrospective study, patients who underwent intracytoplasmic sperm injection (ICSI) treatment with low AMH levels at our infertility clinic were enrolled into the study, retrospectively. All patients had at least 12 months infertility for and had undergone in-

fertility evaluations including medical history and physical and gynecologic examination. Demographic, clinical and ART outcomes of patients were abstracted from hospital database. Patients were divided into two groups as <36 years and  $\geq$  36 years of age. Exclusion criteria were; AMH level >1.0 ng/ml, body mass index (BMI)>35 kg/m<sup>2</sup>, presence of endocrine or metabolic disorders, uterine factor, pelvic inflammatory disease. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the local Ethics Committee of our institute.

### Treatment Protocol

Baseline transvaginal ultrasound was performed all patients at menstrual cycle days 2-3. Ovarian stimulation was started with recombinant FSH (Gonal-F®, Merck Serono, Istanbul, Turkey) with or without human menopausal gonadotropin (hMG; Menogon®; Ferring Pharmaceuticals) and patients underwent either long gonadotropin releasing hormone (GnRH) agonist protocol or GnRH antagonist protocol. The starting gonadotropin dose was determined according to patient's age, BMI, AFC, AMH levels and previous response to gonadotropins. All patients were monitored with ovarian follicular measurements with transvaginal ultrasound and serum estradiol levels. Gonadotropin dose was adopted based on patient's response during the follow up with 1-3 days intervals. In GnRH agonist protocol; 0.5 mg/day dose of long GnRH agonist (leuprolide acetate; Lucrine; Abbott, Turkey) was started at 21th day of the previous menstrual cycle for down-regulation. In antagonist protocol; GnRH antagonist (Cetrotide®; Serono USA) was administered at 0.25 mg subcutaneously daily when a follicle reached 14 mm in diameter or serum E2 level reached >350 pg/mL until the day of oocyte maturation trigger. In both protocol; when the two leading follicles reached  $\geq$ 17 mm in diameter 250 mcg recombinant hCG (Ovitrelle®; Serono USA) was administered to induce ovulation subcutaneously.

Transvaginal ultrasound guided oocyte retrieval was performed 36 hours after trigger injection. The oocytes underwent ICSI with prepared sperm 2–4 h after collection, and fertilization was confirmed 16–18 h later. Embryo transfer was performed on day 3, 4 or 5 based on the quality of embryos. The luteal phase was supported by vaginal progesterone gel (Crinone %8 gel; Serono, Istanbul, Turkey) twice a day.

## Embryo Quality

The polarization, presence of a cytoplasmic halo, number of pronuclei and pronuclear appearance were the morphological features using in zygote scoring system. Embryo quality was described according to the blastomeres size and the number, the degree of fragmentation, and the presence of multinucleated blastomeres. (14, 15).

Chemical pregnancy was defined as positive  $\beta$ -hCG test following embryo transfer. Clinical pregnancy was described as fetal pole and fetal cardiac activity with ultrasonographic examination. Ongoing pregnancy was defined as viable pregnancy with ultrasonographic confirmation at 12 weeks.

## Statistical analysis

Statistical analysis of the data was performed by using SPSS 11.0 software (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL). Categorical variables were analyzed with Chi square tests and continuous variables were analyzed with Mann-Whitney U test where appropriate. Data were presented as mean  $\pm$  standard deviation (sd) or n (%). The level of significance was accepted at  $p=0.05$  level.

## RESULTS

93 patients who underwent ICSI treatment with low serum AMH levels were enrolled into this study. 35.5% (n=33) of patients were  $\geq 36$  years of age and 64.5% (n=60) of patients

**Table 1:** Comparison of the demographic, clinical characteristics of two groups.

	< 36 years (n=60) (mean $\pm$ sd) n,(%)	$\geq 36$ years (n=33) (mean $\pm$ sd) n,(%)	<i>p</i>
Age (years)	31.52 $\pm$ 3.14	37.91 $\pm$ 2.28	0.000
BMI (kg/m <sup>2</sup> )	25.26 $\pm$ 3.41	24.79 $\pm$ 2.39	0.607
Gravida	0.28 $\pm$ 0.74	0.55 $\pm$ 1.43	0.543
Duration of infertility (years)	5.64 $\pm$ 3.62	6.40 $\pm$ 5.15	0.796
Infertility type			
Primary	86.7%	84.8%	0.809
Secondary	13.3%	15.2%	
Basal FSH level (mIU/mL)	8.18 $\pm$ 3.64	9.84 $\pm$ 6.53	0.596
Basal Estradiol level (pmol/L)	48.07 $\pm$ 21.52	53.78 $\pm$ 53.49	0.593
AMH (ng/ml)	0.42 $\pm$ 0.34	0.46 $\pm$ 0.32	0.546
AFC	6.23 $\pm$ 3.29	5.06 $\pm$ 3.01	0.062

Mann Whitney U test or Chi Square test were used where appropriate. The level of significance was accepted at  $p = 0.05$  level, BMI: Body mass index, FSH: Follicle stimulating hormone, AMH: Anti-müllerian hormone, AFC: Antral follicle count.

**Table 2:** Comparison of ART treatment characteristics of two groups.

	< 36 years (n=60) (mean $\pm$ sd) n,(%)	$\geq 36$ years (n=33) (mean $\pm$ sd) n,(%)	<i>p</i>
Ovarian stimulation protocol			
Agonist	11 (18.3)	10 (30.3)	0.204
Antagonist	49 (81.7)	23 (69.7)	
Duration of stimulation (days)	9.25 $\pm$ 3.01	8.50 $\pm$ 2.11	0.376
Total dose of gonadotropin (IU)	3072.92 $\pm$ 1573.61	2766.41 $\pm$ 1202.81	0.602
E2 on hcg day (pmol/L)	926.0 $\pm$ 725.91	942.44 $\pm$ 787.51	0.496
End line (mm)	8.65 $\pm$ 2.06	8.19 $\pm$ 2.13	0.366
Total number of retrieved oocytes	4.07 $\pm$ 2.98	3.33 $\pm$ 3.52	0.080
Total number of MII oocytes	3.38 $\pm$ 2.37	2.76 $\pm$ 2.86	0.070
Total number of embryos	2.15 $\pm$ 1.64	1.45 $\pm$ 1.82	0.015
Number of transferred embryo	0.98 $\pm$ 0.54	0.94 $\pm$ 0.83	0.714
Total number of top quality embryos on day1	0.68 $\pm$ 0.73	0.46 $\pm$ 0.91	0.032
Total number of good quality embryos on day1	1.41 $\pm$ 0.96	1.17 $\pm$ 0.94	0.322
Total number of top quality embryos on day3	0.75 $\pm$ 0.69	0.62 $\pm$ 0.81	0.377
Total number of good quality embryos on day3	1.18 $\pm$ 1.02	0.88 $\pm$ 1.19	0.076

Mann Whitney U test or Chi Square test were used where appropriate. The level of significance was accepted at  $p = 0.05$  level.

were <36 years of age. Demographic and clinical data of two groups were given in Table 1. There were no significant differences between two groups in terms of demographic and clinical features. The characteristics of ART treatment of two groups were compared and given in Table 2. Total numbers of embryos and total numbers of top quality embryos on day1 were significantly higher in women < 36 years of age ( $p_1=0.015$ ,  $p_2=0.032$ ). The other characteristics of ART cycle were similar between two groups. The biochemical, clinical and ongoing pregnancy rates were compared and given Table 3.

The biochemical and clinical pregnancy rates were found similar between two groups. The ongoing pregnancy rates were significantly lower in women  $\geq 36$  years of age ( $p=0.035$ ). The cycle cancellation rates were 1.7% in women < 36 years of age whereas 15.2% in women  $\geq 36$  years of age and the difference was found as statistically significant ( $p=0.011$ ).

**Table 3:** Comparison of pregnancy rates of two groups.

	< 36 years (n=60)	$\geq 36$ years (n=33)	<i>p</i>
Biochemical Pregnancy n,(%)	14 (23.3)	5 (15.2)	0.349
Clinical Pregnancy n,(%)	12 (20.0)	4 (12.1)	0.335
Ongoing pregnancy n,(%)	11 (18.3)	1 (3.0)	0.035

Chi Square test was used. The level of significance was accepted at  $p = 0.05$  level.

## DISCUSSION

In present study, the total numbers of embryos were found significantly higher in women < 36 years of age than in women  $\geq 36$  years of age with low AMH levels. The total number of top quality embryos on day 1 was lower in women  $\geq 36$  years of age than in women < 36 years of age and the difference between two groups showed statistical significance. The biochemical, clinical, and ongoing pregnancy rates of women < 36 years were higher than those of women  $\geq 36$  years of age; however only the ongoing pregnancy rate showed statistical significant difference. The cycle cancellation rates of women < 36 years and women  $\geq 36$  years of age were 1.7% and 15.2%, respectively and the difference was found as statistically significant. In the literature, the prediction value of serum AMH levels for estimation of the poor ovarian response to gonadotropin stimulation in IVF treatment was evaluated in different studies and meta-analyses. In a meta-analysis by Broer et al, the first IVF treatment cycle of 5705 women was evaluated and the authors stated that the single test of AMH had a acceptable value for prediction of the poor ovarian response (16). In a study by Galey-Fontaine et al, the outcomes of IVF/ICSI procedures were analyzed in terms of age and ovarian reserve of women with poor

ovarian response to stimulation. In analyzing of the outcomes of IVF according to age, the outcomes showed difference with a cutoff value at 36 years. The authors reported that the pregnancy rates were found as 14.6% in younger women whereas 4.9% in older women and the difference reached statistical significance (17). Saldeen et al evaluated the pregnancy rates and cycle cancellation rates of patients with poor ovarian response after IVF treatment. The reported pregnancy rates per oocyte pick up for women  $\leq 37$  and  $> 37$  years of age were 14.0% and 3.0%, respectively. In addition, the cycle cancellation rates were stated in women  $\leq 37$  and  $> 37$  years of age were 40.1% and 43.6%, respectively (18). In our study, the ongoing pregnancy rates were 18.3% in women < 36 years of age and 3.0% in women  $\geq 36$  years of age ( $p < 0.05$ ). The cycle cancellation rates were 1.7% in women < 36 years and 15.2% in women  $\geq 36$  years of age ( $p < 0.05$ ).

In a review, Oudendijk et al reported that the effect of female age on outcomes of ART treatment of poor responders was assessed in subgroup analysis of ten different studies. Decline in the pregnancy rates of older poor responders were reported in all ten studies; however five of those studies stated a statistically significant difference. Overall, the pregnancy rates of younger women ranged between 13.0 and 35% whereas the pregnancy rates of older women ranged between 1.5 and 12.7% (9). Age is the one of the most important factors for the prognosis of the IVF outcomes of patients with low AMH levels. The negative effect of age on pregnancy rates is considered particularly related with lower oocyte and embryo quality (9). The outcomes of present study support the previously described possible reason of the worsening effect of age on the prognosis of IVF treatment among poor responders. There was a tendency toward statistical significance between two groups in terms of total numbers of MII oocytes, which were higher in women < 36 years than in women  $\geq 36$  years of age. Besides, the embryo quality was higher in younger women than older women and there was a significant difference between two groups in terms of the total numbers of top quality embryos on day 1.

In conclusion, the higher ongoing pregnancy rates and embryo quality in younger women is an important outcome to encourage the young women with low serum AMH levels for ART treatment option. Age should take into account in the management and information of women with low AMH level in terms of pregnancy rates and characteristics of ART treatment particularly cycle cancellation rates.

## REFERENCES

1. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artensio AC, Stabile G, Volpe A. Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). *Hum Reprod Update* 2010;16:113–130.
2. Broer SL, Mol BW, Hendriks D, Broekmans FJ. The role of anti-Mullerian hormone in prediction of outcome after IVF: comparison with the antral follicle count. *Fertil Steril* 2009;91:705–714.
3. La Marca A, Stabile G, Carducci Artensio A, Volpe A. Serum anti-Mullerian hormone throughout the human menstrual cycle. *Human Reprod (Oxford, England)*. 2006;21(12):3103–7.
4. Nelson SM, Yates RW, Lyall H, Jamieson M, Traynor I, Gaudoin M, Mitchell P, Ambrose P, Fleming R. Anti-Mullerian hormone-based approach to controlled ovarian stimulation for assisted conception. *Hum Reprod* 2009;24:867–875.
5. Broekmans FJ, Kwee J, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF outcome. *Hum Reprod Update* 2006;12:685–718.
6. Anckaert E, Smits J, Schiettecatte J, Klein BM, Arce JC. The value of anti-Mullerian hormone measurement in the long GnRH agonist protocol: association with ovarian response and gonadotrophin-dose adjustments. *Hum Reprod* 2012;27:1829–1839.
7. Stoop D, Ermini B, Polyzos NP, Haentjens P, de Vos M, Verheyen G, et al. Reproductive potential of a metaphase II oocyte retrieved after ovarian stimulation: an analysis of 23 354 ICSI cycles. *Hum Reprod* 2012;27:2030–5.
8. Ferraretti AP et al. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria. *Human Reprod (Oxford, England)*. 2011;26(7):1616–24.
9. Oudendijk JF, Yarde F, Eijkemans MJ, Broekmans FJ, Broer SL. The poor responder in IVF: is the prognosis always poor?: a systematic review. *Hum Reprod Update*. 2012 Jan-Feb;18(1):1-11.
10. Pellestor F, Andreo B, Arnal F, Humeau C, Demaille J. Maternal aging and chromosomal abnormalities: new data drawn from in vitro unfertilized human oocytes. *Hum Genet* 2003; 112:195–203.
11. Baker, V.L., Luke, B., Brown, M.B., Alvero, R., Frattarelli, J.L., Usadi, R., Grainger, D.A. and Armstrong, A.Y. (2010) Multivariate Analysis of Factors Affecting Probability of Pregnancy and Live Birth with in Vitro Fertilization: An Analysis of the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System. *Fertility and Sterility*,94, 1410-1416.
12. Tan, S.L., Royston, P., Campbell, S., Jacobs, H.S., Betts, J., Mason, B. and Edwards, R.G. (1992) Cumulative Conception and Live birth Rates after in-Vitro Fertilization. *The Lancet*, 339, 1390-1394.
13. Beckers, N.G., Macklon, N.S., Eijkemans, M.J. and Fauser, B.C. (2002) Women with Regular Menstrual Cycles and a Poor Response to Ovarian Hyperstimulation for in Vitro Fertilization Exhibit Follicular Phase Characteristics Suggestive of Ovarian Aging. *Fertility and Sterility*, 78, 291-297.
14. Van Royen E, Mangelschots K, De Neubourg D, Valkenburg M, Van de Meerssche M, Ryckaert G, et al. Characterization of a top quality embryo, a step towards single-embryo transfer. *Hum Reprod* 1999;14: 2345–9.
15. Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology. Balaban B, Brison D, Calderon G, Catt J, Conaghan J, et al. The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting. *Hum Reprod* 2011;26:1270–83.
16. Broer SL, van DJ, Broeze KA, Dolleman M, Opmeer BC, Bossuyt P, Eijkemans MJ, Mol BW, Broekmans FJ. Added value of ovarian reserve testing on patient characteristics in the prediction of ovarian response and ongoing pregnancy: an individual patient data approach. *Hum Reprod Update* 2013;19:26–36.
17. Galey-Fontaine J, Cédric-Durnerin I, Chaïbi R, Massin N, Hugues JN. Age and ovarian reserve are distinct predictive factors of cycle outcome in low responders. *Reprod Biomed Online*. 2005 Jan;10(1):94-9.
18. Saldeen P, Kallen K, Sundstrom P. The probability of successful IVF outcome after poor ovarian response. *Acta Obstet Gynecol Scand* 2007;86:457–461.

## Benign Endikasyonlarda Laparoskopik ve Abdominal Histerektomi

### Comparison of Laparoscopic and Abdominal Hysterectomy for Benign Diseases

Emine Öztürk <sup>1</sup>, Hakan Güraslan <sup>2</sup>, Keziban Doğan <sup>2</sup>, Mehmet Baki Şentürk <sup>3</sup>  
 Birgül Güraslan <sup>2</sup>, Nadire Sevda İdil <sup>2</sup>, Levent Yaşar <sup>2</sup>

1. Bahçelievler Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, Türkiye

2. Bakırköy Dr Sadi Konuk Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, Türkiye

3. Zeynep Kamil Kadın ve Çocuk Hastalıkları EAH, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, Türkiye

#### ÖZET

**Amaç:** Bu çalışmanın amacı benign endikasyonlarla yapılan histerektomilerde laparoskopik yaklaşım ile abdominal yaklaşımın intraoperatif ve kısa dönem postoperatif komplikasyonlarını karşılaştırmaktır.

**Gereç ve Yöntem:** Bu retrospektif kohort çalışmasında Ocak 2011-Aralık 2013 tarihleri arasında benign nedenlerle total abdominal ve laparoskopik histerektomi yapılan 253 hastanın orijinal dosyaları ve ameliyat raporları analiz edildi. İki ayrı histerektomi yaklaşımı operasyon süresi, kan kaybı, majör komplikasyonlar ve hastanede yatış süresi açısından karşılaştırıldı.

**Bulgular:** Toplam 253 hastanın 151 tanesine (%60) abdominal, 102 (%40) tanesine laparoskopik histerektomi yapılmıştır. Operasyon süresi laparoskopik histerektomi grubunda anlamlı olarak daha uzun saptandı ( $p = 0,001$ ). Majör komplikasyonlar açısından laparoskopik histerektomi ile abdominal histerektomi arasında fark saptanmadı ( $p = 0,560$ ). Postoperatif hemoglobin düşüşü TAH grubunda daha fazlaydı ( $p = 0,031$ ). Hastanede yatış süresi laparoskopik histerektomi grubunda anlamlı olarak daha kısaydı ( $p = 0,004$ ). Laparoskopik histerektomi de laparotomiye dönme oranı %12 olarak saptandı.

**Sonuç:** Laparoskopik histerektomi abdominal histerektomiye oranla kısa iyileşme periyodu, daha az postoperatif rahatsızlık, daha iyi kozmetik sonuçlar gibi birçok avantaja sahiptir. Her iki yaklaşımdaki majör komplikasyon oranı benzerdir. Vajinal histerektominin uygun olmadığı hastalarda laparoskopik yaklaşım abdominal yaklaşıma tercih edilmelidir.

**Anahtar Kelimeler:** kan kaybı; endoskopi; jinekolojik cerrahi; histerektomi; laparoskopi

#### ABSTRACT

**Objective:** The aim of this study was to compare the intraoperative and short term postoperative complications between the abdominal and laparoscopic hysterectomies for women with benign disease.

**Material and Method:** In this retrospective cohort study, we analyzed the files of the 253 patients who underwent total abdominal or laparoscopic hysterectomy for benign conditions in our clinic between January 2011 and December 2013. The operating time, blood loss, the major complication rate and the duration of hospital stay were compared between the abdominal and the laparoscopic hysterectomy groups respectively.

**Results:** Among the total of the 253 patients, hysterectomy was performed abdominally for 151 (60%) patients and laparoscopically for the 102 (40%) patients. The operating time was found to be significantly longer for the laparoscopic approach ( $p = 0.001$ ). No statistically significant difference was found between the groups for the major complication rate ( $p = 0.560$ ). Postoperative decline for hemoglobin levels in the abdominal hysterectomy group was higher than in the laparoscopic group ( $p = 0.031$ ). The duration of hospital stay was found to be shorter in the laparoscopic group ( $p = 0.004$ ). The conversion rate to open surgery was 12%.

**Conclusion:** Laparoscopic hysterectomy has more advantages than abdominal hysterectomy when compared for time needed for postoperative recovery, abdominal discomfort after surgery and cosmetically results. The major complication rates were similar for the two approaches. When vaginal approach is not appropriate for the patient, laparoscopic hysterectomy should be considered as the first option for the surgery.

**Keywords:** blood loss; endoscopy; gynecologic surgery; hysterectomy; laparoscopy

#### İletişim Bilgileri:

**Sorumlu Yazar:** Hakan Güraslan

**Yazışma Adresi:** Dr Sadi Konuk EAH, Kadın Hast. ve Doğ. Kl. Tevfik Sağlam Cad. No:11 Zuhuratbaba, Bakırköy 34147, İstanbul

**E-posta:** guraslanhakan@gmail.com

**Tel:** +90 (532) 23710 03

**Makalenin Geliş Tarihi:** 06.09.2015

**Makalenin Kabul Tarihi:** 20.03.2016

**DOI:** <http://dx.doi.org/10.16948/zktb.40306>

## GİRİŞ

Laparoskopik histerektomi kısa hospitalizasyon, daha az intraoperatif kan kaybı, daha az postoperatif ağrı, hızlı iyileşme ve daha düşük infeksiyon oranları sunar, ancak uygulanma oranları halen abdominal histerektominin çok altındadır [1]. Amerika Birleşik Devletlerinde 2010 yılında histerektomilerin % 54.2 si abdominal yolla yapılırken sadece %8.6 sı laparoskopik yapılmıştır [2]. Ülkemizde de durum farklı değildir. Laparoskopik cerrahide önde gelen merkezlerimizde bile abdominal histerektomi oranları laparoskopik histerektominin çok üstündedir [3]. Bu laparoskopik yaklaşımda başta üriner olmak üzere majör komplikasyon oranının daha yüksek olması ve laparoskopik histerektominin öğrenme eğrisinin daha uzun olması ile açıklanabilir.

Benign endikasyonlarda histerektomi için en uygun cerrahi yaklaşımın değerlendirildiği 2015 Cochrane derlemesinin sonuçlarına göre vaginal histerektomi abdominal ve laparoskopik yaklaşımdan üstündür ve ilk tercih olmalıdır. Vajinal histerektominin uygun olmadığı hastalarda abdominal histerektomiden kaçınmak için laparoskopik yaklaşım önerilebilir, ancak laparoskopik histerektominin daha fazla üriner yol komplikasyonları ile ilişkili olduğu dikkate alınmalıdır [4]. Metaanalizlerin aksine deneyimli ellerde laparoskopik histerektominin majör komplikasyon oranını arttırmadığını rapor eden geniş serili çalışmalar da vardır [5, 6].

Biz bu makalede kliniğimizde benign endikasyonlarla yapılan 253 total abdominal ve laparoskopik histerektomi olgusunu sunuyoruz. Bu çalışmanın amacı abdominal ve laparoskopik histerektomide komplikasyon oranlarını değerlendirmektir.

## GEREÇ ve YÖNTEM

Ocak 2011 - Aralık 2013 tarihleri arasında, Bakırköy Dr Sadi Konuk Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniğinde histerektomi yapılan 437 hasta retrospektif olarak gözden geçirildi. Malignite nedeniyle histerektomi yapılan 112, postpartum kanama nedeniyle sezeryan histerektomi yapılan 2, supraservikal ve laparoskopik asiste vajinal histerektomi yapılan 47 hasta ile kayıtları eksik olan 23 hasta çalışma dışı bırakıldı.

Tüm hastaların orjinal dosyaları, anestezi kayıtları ve operasyon notları analiz edildi. Yaş, kilo, boy, parite, menapozal durum, sezeryan ve diğer abdominal cerrahi öyküsü, histerektomi endikasyonu kayıt edildi.

Primer sonuçlar operasyon süresi, major komplikasyon oranı, postoperatif hemoglobin düşüş oranı ve hastanede yatış süresi olarak belirlendi. İntraoperatif tahmini kan kaybını belirten objektif bir ölçüm yapılmamıştı. Bu nedenle kanama paterni değerlendirmesi için operasyon sonrası hemoglobindeki düşüş dikkate alındı.

Operasyon süresi ilk cilt insizyonu ile insizyonun tamamen kapatılması arasındaki süre olarak tanımlandı. Hemoglobin değerleri için operasyondan 12 saat önce ve 24 saat sonraki ölçümler kaydedildi. Operasyon tarihinden taburcu tarihine kadar geçen süre hastanede kalış süresi olarak kabul edildi. Tüm hastalara operasyondan 1 saat önce, Sefazolin 1 gr İV olarak uygulanmış ve postoperatif 12. saatte aynı doz tekrarlanmıştı. Tromboemboli profilaksisi için operasyondan 8 saat önce Enoxaparin 0.4 ml S.C uygulandığı ve yatış boyunca 24 saat arayla devam edildiği görüldü.

İstatistiksel analizler NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) paket programı ile yapıldı. Verilerin değerlendirilmesinde tanımlayıcı istatistiksel metotların (ortalama, standart sapma) yanı sıra ikili grupların karşılaştırmasında bağımsız t testi, operasyon öncesi ve operasyon sonrası değişkenlerin değerlendirilmesinde eşlendirilmiş t testi, normal dağılım göstermeyen parametrelerde Mann-Whitney U testi, nitel verilerin karşılaştırmalarında ki-kare ve uygun olduğu yerde Fisher gerçeklik testi kullanıldı. Anlamlılık  $p < 0,01$  ve  $p < 0,05$  düzeylerinde değerlendirildi.

**Histerektomi Prosedürü:** Kliniğimizde total laparoskopik histerektomi ve total abdominal histerektomi tekniği tüm hastalara aşağıda tanımlandığı gibi uygulanmaktadır.

**TLH prosedürü:** Batına umblikusun tam ortasından kapalı teknikte ve 90 derece açı ile girilip pnömoperitoneum oluşturulduktan sonra kamera için umblikustan 10 mm port (10 mm trochar; Ethicon Endo-Surgery, Cincinnati, OH, USA) girilir. İki tanesi spina iliaka anterior superiorun 2 cm medialine, bir tanesi suprapubik olmak üzere üç adet 5 mm port (Ethicon Endo-Surgery) direkt görüş altında girilir. Uterus manipülasyonu için Clermont-Ferrand uterin manüplatör (Karl Storz, Tuttlingen, Germany) yerleştirilir.

Operasyona 5 mm harmonic scalpel (Ethicon Endo-Surgery) ile ligamentum rotundumlar yakılıp kesilerek başlanır. Ligamentum latumda pencere açılarak ureter uzaklaştırıldıktan sonra, ya da ureterler sadece periton dışından

gözleneren EnSeal ile (Ethicon Endo-Surgery) infundibulopelvik ligament ya da utero-ovarian ligament koagüle edilerek kesilir. Broad ligamentin arka yaprağı uterusakral ligamente doğru disseke edilir. Uterus önünde periton harmonic scalpel ya da bipolar koter ve makas ile açılarak mesane serviks ön yüzünden vajene doğru uzaklaştırılır. Uterin arterlerler EnSeal ile koagüle edildip kesildikten sonra, serviko-vajinal bileşmeden harmonic scalpel ile kesilerek piyes çıkarılır. Vajen kafi laparoskopik olarak V-loc™ (Covidien, Dublin, Ireland) sütür ile kapatılır.

**TAH prosedürü:** Operasyona uterusun büyüklüğüne göre simfiz üstünden transvers ya da median insizyonla batına girilerek başlanır. Abdominal kavite eksplere edildikten sonra ligamentum rotundumlar kesilip bağlanır. Periton infundibulopelvik ligamente doğru açıldıktan sonra ya periton dışından ya da retroperitoneal alana girilerek bilateral ureterler belirlenir. Aynı şekilde ligamentum latumda pencere açılarak ureterler uzaklaştırılır. Uteroovaryan ya da infundibulopelvik ligamentler kesilip bağlanır.

Mesane uterus ön yüzünden uzaklaştırıldıktan sonra uterin arterler kesilip bağlanır. Önden ya da yandan vajene girilerek piyes çıkarıldıktan sonra vaginal cuff 1 numara absorbabl sütürle kontinü kapatılır.

## BULGULAR

Çalışmaya 151 tanesi TAH, 102 tanesi TLH olmak üzere toplam 253 hasta kaydedildi. Hastaların ortalama yaşı  $49 \pm 7$  (34-89) ortalama vücut kitle indeksi  $30 \pm 4$  (21-49) idi. Parite, preoperatif hemoglobin değeri, geçirilmiş sezeryan ve abdominal cerrahi öyküsü açısından gruplar arasında fark yoktu. TLH grubunda ortalama vücut kitle indeksi ( $32 \pm 6$ ) TAH grubundan ( $29 \pm 3$ ) daha yüksekti ( $p < 0.001$ ). Ortalama yaş, ve postmenapozal hasta oranı da TLH grubunda anlamlı olarak daha yüksekti ( $p < 0.001$ ) (Tablo 1).

**Tablo 1:** TLH ve TAH olgularının demografik özellikleri.

	TAH n=151	TLH n=102	p
Yaş (y)	47 ± 4	52 ± 9	<0.001**
BMI (kg/m <sup>2</sup> )	29 ± 3.2	32 ± 6.1	<0.001**
Menapoz durumu	35 (23.2%)	64 (62.7%)	<0.001**
Parite	3 ± 1.2	2.9 ± 1.9	0.964
C/S	15 (9.9%)	9 (8.8%)	0.768
Abdominal cerrahi öyküsü	15 (9.9%)	17 (16.7%)	0.114

\*  $p < 0.05$ , \*\*  $p < 0.01$

Histerektomi yapılan hastalarda iki grupta da en sık endikasyon leiomyomdu (65%). Ancak TAH grubunda leiomyoma oranı (82%) TLH grubundan (40%) fazlayken, endometrial hiperplazi, endometrial polip, servikal displazi ve adneksiyal kitle endikasyonları TLH grubunda daha sıkı (Tablo 2).

**Tablo 2:** TLH ve TAH olgularında endikasyonlar.

	TAH N=151	TLH N=102	Total N=253	p
Leiomyoma	123 (81.5%)	41 (40.2%)	164 (64.8%)	< 0.001**
Anormal uterin kanama	17 (11.3%)	15 (14.7%)	32 (12.6%)	0.420
Endometrial hiperplazi	5 (3.3%)	25 (24.5%)	30 (11.9%)	< 0.001**
Endometrial polip		4 (3.9%)	4 (1.6%)	0.025*
Servikal displazi		5 (4.9%)	5 (2%)	0.01**
Kronik pelvik ağrı	2 (1.3%)	3 (2.9%)	5 (2%)	0.651
Adneksiyal kitle		6 (5.9%)	6 (2.4%)	0.004**
Uterin prolapsus	4 (2.6%)	1 (1%)	5 (2%)	0.417
Tubeovaryan abse		2 (2%)	2 (0.8%)	0.162

\*  $p < 0.05$ , \*\*  $p < 0.01$

TAH grubunda ortalama operasyon süresi (118 dak, aralık 60-240), TLH grubundan (131 dak, aralık 75-235) daha kısa idi ( $p = 0.001$ ). Postoperatif 1. gün hemoglobin değerindeki düşüş TAH grubunda daha yüksekti ( $p = 0.031$ ). Ancak transfüzyon gereksinimi olan hasta sayısı açısından TAH (22 hasta) ve TLH (9 hasta) grupları arasında fark yoktu ( $p = 0.171$ ). Hastanede yatış süresi TLH yapılan hastalarda anlamlı olarak daha kısaydı ( $p = 0.004$ ) (Tablo 3).

**Tablo 3:** TAH ve TLH olgularında operatif ve postoperatif bulgular.

	TAH	TLH	p
Operasyon süresi (dk)	118 ± 25	131 ± 31	< 0.001**
Yatış süresi (gün)	2.9 ± 1.2	2.5 ± 1.3	0.004**
Preoperatif hb (g/dL)	10.8 ± 1.5	11 ± 1.5	0.346
Postoperatif hb (g/dL)	9.6 ± 1.4	10.2 ± 1.5	0.002**
Postoperatif hb düşüşü (%)	9.8 ± 8	7.4 ± 9.6	0.031*
Uterus ağırlığı (g)	409 ± 360	200 ± 114	< 0.001**

\*  $p < 0.05$ , \*\*  $p < 0.01$

TAH yapılan hastaların 6% sında ( $n = 9$ ), TLH yapılanların 8% inde ( $n = 8$ ) majör komplikasyon olduğu görüldü ( $p = 0.560$ ). TLH grubundaki 8 majör komplikasyonun 5 tanesi çalışmamızın ilk yılına aitti. Üç tanesi TAH grubunda 3 tanesi TLH grubunda olmak üzere 6 hastada barsak yaralanması olmuştu. TLH grubundaki 1 barsak yaralanması Palmer noktasından batına giriş sırasında oluşmuş, mini