Should we add unilateral sacrospinous ligament fixation to vaginal hysterectomy in management of stage 3 and stage 4 pelvic organ prolapse?

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Abstract

Objective: To compare “vaginal hysterectomy alone” with “vaginal hysterectomy with prophylactic unilateral sacrospinous ligament fixation” in terms of intraoperative complications and 1-year anatomic outcomes and symptoms in patients aged over 50 years who presented with stage 3 or 4 pelvic organ prolapse (POP).

Materials and Methods: Thirty-five patients underwent vaginal hysterectomy alone and 32 patients underwent vaginal hysterectomy with unilateral sacrospinous ligament fixation because of benign pathology between January 2012, and June 2014, were retrospectively analyzed in this study. The patients’ demographic data and preoperative and intraoperative findings were obtained from the hospital records and noted. The patients were invited by phone to a follow-up visit to assess their 1-year anatomic outcomes and symptoms.

Results: There was no significant demographic difference between the patients who underwent vaginal hysterectomy alone and those who had a vaginal hysterectomy with sacrospinous ligament fixation. Both length of operation and hospital stay were significantly longer in the patients who underwent vaginal hysterectomy with sacrospinous ligament fixation (p<0.001); intraoperative complications requiring blood transfusion were also significantly more frequent in these patients compared with the patients who underwent vaginal hysterectomy only (p=0.048). Recurrence of vaginal vault prolapse was significantly more frequent in the patients with vaginal hysterectomy alone compared with those who had both vaginal hysterectomy and sacrospinous ligament fixation (p=0.035).

Conclusion: Unilateral sacrospinous ligament fixation might be added to vaginal hysterectomy in patients with stage 3 or 4 POP who are predicted to have long survival times. However, further studies with a larger sample size are needed in this area of research.

Keywords: Pelvic organ prolapse, vaginal hysterectomy, sacrospinous ligament fixation

Öz

Amaç: Bu çalışmada amacımız 50 yaş üzeri evre 3-4 pelvik organ prolapsusu (POP) olan hastalarda profilaktik unilateral sakrospinöz ligament fixasyonu yapılan ve yapılmayan vajinal histerektomi olgularının intraoperatif komplikasyonlarını, uzun dönem anatominik sonuçlarını ve semptomlarını karşılaştırmaktır.

Gereç ve Yöntem: Ocak 2012-Haziran 2014 tarihleri arasında, benign patoloji nedeniyle sadece vajinal histerektomi uygulanan 35 hasta ve vajinal histerektomi+unilateral sakrospinöz ligament fixasyonu uygulanan 32 hasta çalışmaya dahil edildi. Hastaların demografik bulguları, preoperatif prolapsus bulguları, intraoperatif bulguları hastane kayıtlarından ele edildi. Bir yıllık anatominik sonuçlar ve semptomlar için hastalar telefonla aranarak kontrol edildi.

Bulgular: Vajinal histerektomi ve vajinal histerektomi+sakrospinöz ligament fixasyonu yapılan 2 grup hastanın demografik bulguları arasında anlamlı bir fark tespit edilemedi. Operasyon süreleri ve hastanede kalan süreleri vajinal histerektomi+sakrospinöz ligament fixasyonu grubunda anlamlı olarak daha uzun tespit edildi (p<0.001). Intraoperatif komplikasyonlardan transfüzyon gerektiren kanama vajinal histerektomi+sakrospinöz ligament fixasyonu grubunda
Introduction

Pelvic organ prolapse (POP) affects approximately 50% of women aged over 50 years. Its lifetime prevalence is 30-50%. Approximately 11-12% of all women undergo surgery for pelvic floor dysfunction before they reach 80 years of age(1). Uterovaginal prolapse is a serious health issue that especially occurs in women with a history of vaginal delivery. The incidence of uterovaginal and vaginal vault prolapse is observed to be particularly high among the elderly because pelvic floor structures loosen with age. The etiology of uterovaginal prolapse involves pregnancy, delivery, lifting heavy weights, obesity, increased intra-abdominal pressure because of such factors as pelvic masses, and weakened pelvic floor structures(2). The surgical therapy that is typically adopted in this health issue is vaginal hysterectomy. Various therapeutic techniques have been suggested to be performed at the time of vaginal hysterectomy to avoid potential recurrence of prolapse. However, it remains unclear which of the therapeutic techniques is superior(3).

Several surgical techniques have been suggested to be performed at the time of vaginal hysterectomy to avoid potential recurrence of prolapse. Of these, vaginal techniques are the most frequently adopted because of the following advantages: shorter length of operation, faster healing, and lower rates of adhesion. Sacrospinous ligament fixation (SLF) is one of these techniques(4,5). In brief, SLF refers to suspension of the vaginal vault from the sacrospinous ligament, which extends from the ischial spine, to the coccyx and the lower portion of the sacrum. This technique was first defined by Sederl in 1958. It allows for suspension of the vagina from the sacrospinous ligament, thereby bringing it to a level above the levator ani muscle.

The aim of this study was to compare "vaginal hysterectomy with prophylactic unilateral SLF" with "vaginal hysterectomy alone" in terms of intraoperative complications and 1-year anatomic outcomes and symptoms in patients aged over 50 years who presented with stage 3 or 4 pelvic organ prolapse.

Materials and Methods

This study was conducted in Dicle University Faculty of Medicine, Department of Gynecology and Obstetrics upon provision of ethical approval. Fifty patients who had undergone vaginal hysterectomy alone (VH group) and 50 who had undergone vaginal hysterectomy with SLF (VH+SLF group) because of benign pathologies between January 2012, and June 2014, were retrospectively analyzed. Patients aged 50 years and older and staged as stage 3-4 POP according to the POPQ classification system were included in the study (Table 1). Patients with stage 1-2 POP, those who had connective tissue diseases, cancer, immobility, and massive obesity were excluded from the study.

Obesity-BMI ≥30 kg/m²; class 1-BMI of 30.0 to 34.9; class 2-BMI of 35.0 to 39.9 kg/m²; and class 3-BMI ≥40 kg/m². This type of obesity is also referred to as severe, extreme, or massive obesity(6). The patients’ demographic data and preoperative and intraoperative findings were obtained from the hospital records. Data on reasons for presentation to hospital, age at operation, vaginal parity, medical problems, menopausal status, history of operations, stage of prolapse, type and length of operation, length of hospital stay, intraoperative complications (bleeding that required blood transfusion, rectal and bladder injuries, febrile morbidity, and nerve injuries), and 1-year anatomic outcomes (vaginal vault prolapse, cystocele, rectocele, dyspareunia, chronic constipation, abdominal pain and urinary incontinence) were noted. The patients were requested to visit the hospital for follow-up in postoperative week 6 and at 1 year. No-show patients were called by phone and invited to the hospital such that we could assess their 1-year surgical outcomes. Two (4%) patients in the VH group and 3 (6%) from the VH+SLF had died in the meantime of various systemic diseases. Furthermore, 9 (18%) VH patients and 13 (26%) VH+SLF patients could not be reached by phone. In addition, 4 (8%) VH patients and 2 (4%) VH+SLF patients stated that they would not be able to come to the follow-up visit because of long journey distances to the hospital. In total, 33 patients were lost to follow-up, and the remaining 67 patients with 1-year follow-up data were included in the study (35 VH patients and 32 VH+SLF patients).

A total of 67 postmenopausal patients with stage 3 (the most distal portion of the prolapse protrudes more than 1 cm below the hymen but no farther than 2 cm less than the total vaginal length) or 4 (vaginal eversion is essentially complete) pelvic organ prolapse were included in this study. POP staging was done according to POPQ classification system (Table 1)(7).

Points and landmarks for POPQ system examination. Aa; point A anterior, Ap; point A posterior, Ba; point B anterior, Bp; point B posterior; C; cervix or vaginal cuff, D; posterior fornix (if cervix is present), gh; genital hiatus, pb; perineal body, tvl; total vaginal length. Indications for hysterectomy were identified using the criteria defined by Dicker(8).

Surgical technique

The patients were reexamined under anesthesia in a lithotomy position after cleansing the surgical site and positioning sterile drapes. The patients then underwent vaginal hysterectomy, which was followed by a preliminary repair for stage 3 or 4
uterovaginal prolapse. The patients with stress incontinence additionally underwent transobturator tape (TOT) procedures. Then, unilateral SLF was performed (using the technique defined by Nichols)(4) as follows: after the rectovaginal space was opened to the vaginal apex, the right pararectal space was entered using blunt dissection; the ischial spine was palpated and taken as the reference to pinpoint the sacrospinous ligament, which extends from the ischial spine medially to the coccyx and the lower portion of the sacrum. The pararectal fascia was penetrated, and the space was enlarged using blunt dissection; the rectum was retracted to the left using two Breisky-Navratil retractors, thereby exposing the sacrospinous ligament. No 1 non-absorbable suture (Prolene) was placed 2-2.5 cm medially to the ischial spine, and one end of the suture was passed through the vaginal vault; surplus tissue located in the posterior vaginal wall was excised, and the upper 1/3 of the vaginal mucosa was repaired. Following the vaginal vault repair, the vaginal vault was suspended from the right sacrospinous ligament by tying together the sacrospinous sutures located proximal to the apex of the vaginal vault. Lastly, posterior repair and perineoplasty were performed, which marked the end of the procedure. The decision of adding SLF or not to the vaginal hysterectomy was made according to the criteria used by Cruikshank et al.(9) total prolapse uterosacral-cardinal ligament, descent of the vaginal apex to the introitus or lower when pulled after hysterectomy and total plastic operations, and the presence of total procedentia. All surgeries were performed by expert physicians.

**Statistical analysis**

All statistical analyses were performed using SPSS version 11.5. Chi-Square test and Fischer's Exact test (2x2 Tables) were used for comparison of categorical variables. Student's t-test was used for comparison of continuous variables that demonstrated normal distribution, and Mann-Whitney U test was used for comparison of those that did not demonstrate normal distribution. Data were expressed in mean + standard deviation. A p value smaller than 0.05 was considered statistically significant.

**Results**

A total of 67 patients were included in this study; 35 (70%) underwent vaginal hysterectomy alone and 32 (64%) patients underwent vaginal hysterectomy with SLF. The patients' demographic data are shown in Table 2. There were no statistically significant differences between the two groups in age, parity, sexual activity, medical problems, and reasons for presentation to hospital. All of the patients were postmenopausal. Data on preoperative stages of prolapse are reported in Table 3. Both preoperative uterine prolapse + cystocele and preoperative 3rd degree cystocele were significantly more frequent in the VH group (p=0.01 and p=0.015, respectively). The frequency of preoperative 3rd degree rectocele was significantly higher in the VH+SLF group (p=0.006). Anterior colporrhaphy was significantly more frequent in the VH group (p=0.038), whereas posterior colporrhaphy was significantly more frequent in the VH+SLF group (p=0.017). Comparisons between the groups in terms of type, length of operation, and length of hospital stay are demonstrated in Table 4. Both length of operation and hospital stay were significantly longer in the VH+SLF group (p=0.000). Intraoperative complications are shown in Table 5. In this respect, bleeding that required blood transfusion was significantly more frequent in the VH+SLF group (p=0.048). One-year complications were documented in Table 6. Of which, recurrence of vaginal vault prolapse was significantly more frequent in the VH group (p=0.035).

**Discussion**

In this study, intraoperative complications and 1-year anatomic outcomes and symptoms were investigated in patients who underwent vaginal hysterectomy alone as well as in patients who underwent vaginal hysterectomy with SLF. The purpose of the study was to provide an answer to the question “Should we add prophylactic unilateral SLF to vaginal hysterectomy in management of patients with stage 3 or 4 pelvic organ prolapse?” Several studies in the literature have investigated the outcomes of SLF; however, the literature lacks studies that compare vaginal hysterectomy alone with vaginal hysterectomy with SLF.

In a previous study, the authors compared SLF with total mesh and found higher blood loss in patients who underwent SLF(10). Colombo and Milani compared SLF with McCall culdoplasty and found that the latter yielded better results in terms of length of operation, blood loss, and recurrence of prolapse(11). In addition, Maher et al.(12) compared iliococcygeus fixation with

**Table 1. POPQ classification system**

| POPQ classification system | Stage 0 no prolapse is demonstrated. |
| Stage 1 the most distal portion of the prolapse is more than 1 cm above the level of the hymen. |
| Stage 2 the most distal portion of the prolapse is 1 cm or less proximal or distal to the hymenal plane. |
| Stage 3 the most distal portion of the prolapse protrudes more than 1 cm below the hymen but no farther than 2 cm less than the total vaginal length (for example, not all of the vagina has prolapsed). |
| Stage 4 vaginal eversion is essentially complete. |
SLF and found similar results in the two groups of patients in terms of gluteal pain, hemorrhage, and recurrence of prolapse. In agreement with the literature, the present study demonstrated that patients who underwent VH+SLF had significantly higher blood loss compared with those who underwent vaginal hysterectomy alone. Significantly higher blood loss in SLF might be explained by the fact that the surgical site is narrow, and the hypogastric venous plexus and the pudendal vasculature are located in proximity to the sacrospinous ligament. In this respect, firm vaginal tampons, arterial ligation, and hemoclips might be considered in management of hemorrhage\(^{(13)}\). In the present study, 6 (18.8%) of the women who had VH+SLF had hemorrhage. In one (3.1%) of these patients, hemorrhage occurred in the obturator vessels during the TOT procedure.

### Table 2. Patients' demographic data

|                        | Vaginal hysterectomy | Vaginal hysterectomy + sacrospinous ligament fixation | p value |
|------------------------|----------------------|------------------------------------------------------|---------|
| Age                    | 68.3±12.2            | 72.0±12.5                                            | 0.224   |
| Parity                 | 8.4±3.0              | 8.9±2.7                                              | 0.504   |
| Sexually active        |                      |                                                      |         |
| No                     | 17 (48.6%)           | 18 (56.2%)                                           | 0.051   |
| Yes                    | 18 (51.4%)           | 14 (43.8%)                                           |         |
| Medical problems       |                      |                                                      |         |
| None                   | 17 (48.6%)           | 21 (65.6%)                                           |         |
| Smoking                | 6 (17.1%)            | 7 (21.9%)                                            |         |
| Chronic lung disease   | 3 (8.6%)             | 1 (3.1%)                                             | 0.054   |
| Obesity                | 3 (8.6%)             | 1 (3.1%)                                             |         |
| Chronic constipation   | 2 (5.7%)             | 1 (3.1%)                                             |         |
| Others                 | 4 (11.4%)            | 1 (3.1%)                                             |         |
| Reasons for presentation to hospital | | | |
| Prolapsed uterus       | 21 (60%)             | 17 (53.1%)                                           |         |
| Prolapsed bladder      | 6 (17.1%)            | 0                                                     |         |
| Abdominal pain + Chronic constipation + Prolapsed uterus | 4 (11.4%) | 3 (9.4%) | 0.155 |
| Urinary incontinence + prolapsed uterus | 4 (11.4%) | 12 (37.5%) | |

Data were expressed in means ± standard deviations. Chi-Square and Fischer's Exact test were used for categorical variables.

### Table 3. Preoperative degree of prolapse

|                        | Vaginal hysterectomy | Vaginal hysterectomy + sacrospinous ligament fixation | p value |
|------------------------|----------------------|------------------------------------------------------|---------|
| Preoperative organ prolapse |                      |                                                      |         |
| UP + Cystocele         | 9 (25.8%)            | 1 (3.1%)                                             | 0.010   |
| UP + Rectocele         | 1 (2.8%)             | 4 (12.5%)                                            | 0.136   |
| UP + Cystorectocele    | 25 (71.4%)           | 27 (84.4%)                                           | 0.208   |
| Preoperative degree of uterine prolapse | | | |
| 3                      | 8 (22.9%)            | 7 (21.9%)                                            | 0.925   |
| 4                      | 27 (77.1%)           | 25 (78.1%)                                           | 0.647   |
| Preoperative degree of cystocele | | | |
| 1                      | 1 (2.9%)             | 6 (18.7%)                                            | 0.035   |
| 2                      | 0                    | 1 (3.1%)                                             | 0.296   |
| 3                      | 34 (97.1%)           | 25 (78.1%)                                           | 0.015   |
| Preoperative degree of rectocele | | | |
| 1                      | 8 (22.9%)            | 2 (6.2%)                                             | 0.037   |
| 2                      | 1 (2.9%)             | 0                                                     | 0.343   |
| 3                      | 23 (65.8%)           | 30 (93.8%)                                           | 0.006   |

UP: Uterine prolapse. Chi-Square and Fischer's Exact test were used for categorical variables. P values indicate comparison of preoperative degree of prolapse between vaginal hysterectomy group and vaginal hysterectomy + sacrospinous ligament fixation group. P<0.05 was considered statistically significant.
The patients with hemorrhage received spongostan. The content of 2 ampoules of solution was poured on gauze soaked with Transamin 5%, and tamponation was performed. In the present study, one (3.1%) of the VH+SLF patients experienced perineal nerve injury, which resulted in drop foot, because of surgical positioning. This patient was referred to the department of physical therapy and rehabilitation. The patient’s first-year follow-up revealed that impairment of pain sensation in the foot was minimal. The sciatic nerve and its branching perineal nerves can be damaged during lengthy

### Table 4. Types and duration of operations and length of stay

|                          | Vaginal Hysterectomy | Vaginal Hysterectomy + sacrospinous ligament fixation | p value |
|--------------------------|----------------------|------------------------------------------------------|---------|
| Types of operations performed |                      |                                                      |         |
| Ant. Colp.               | 12 (34.3%)           | 4 (12.5%)                                           | 0.038   |
| Post. Colp.             | 1 (2.9%)             | 7 (21.9%)                                           | 0.017   |
| Ant. Colp + Post. Colp  | 22 (62.6%)           | 20 (62.5%)                                          | 0.976   |
| TOT                     | 20 (57.1%)           | 12 (37.5%)                                          | 0.303   |
| Duration of operation (min) | 71.4±18.2           | 99.2±29.6                                           | 0.000   |
| Length of stay (days)   | 2.2±1.0             | 3.9±2.5                                             | 0.000   |

Ant. Colp: Anterior colporrhaphy, Post. Colp: Posterior colporrhaphy, TOT: Transobturator tape procedure, Min: Minute. Data were expressed in means ± standard deviations. Chi-Square and Fischer's Exact test were used for categorical variables. P values: P values indicate comparison of types and duration of operations and length of stay between vaginal hysterectomy group and vaginal hysterectomy + sacrospinous ligament fixation group. P<0.05 was considered statistically significant.

### Table 5. Intraoperative complications

|                               | Vaginal hysterectomy | Vaginal hysterectomy + sacrospinous Ligament fixation | p value |
|-------------------------------|----------------------|-------------------------------------------------------|---------|
| Hemorrhage (requiring blood transfusion) | 1 (2.9%)             | 6 (18.8%)                                             | 0.048   |
| Rectal injury                 | 0                    | 2 (6.2%)                                              | 0.224   |
| Febrile morbidity             | 4 (11.4%)            | 7 (21.9%)                                             | 0.252   |
| Bladder injury                | 2 (5.8%)             | 0                                                     | 0.173   |
| Perineal nerve injury         | 1 (2.9%)             | 0                                                     | 0.478   |

Fischer’s Exact test was used for categorical variables. P values: P values indicate comparison of intraoperative complications between vaginal hysterectomy group and vaginal hysterectomy + sacrospinous ligament fixation group. P<0.05 was considered statistically significant.

### Table 6. One year follow-up anatomic outcomes and symptoms

|                                      | Vaginal hysterectomy | Vaginal hysterectomy + sacrospinous ligament fixation | p value |
|--------------------------------------|----------------------|-------------------------------------------------------|---------|
| Prolapsed vaginal vault             | 7 (20%)              | 1 (3.1%)                                              | 0.035   |
| Cystocele                            | 4 (11.4%)            | 5 (15.6%)                                             | 0.621   |
| Rectocele                            | 1 (2.9%)             | 1 (3.1%)                                              | 0.950   |
| Dyspareunia                          | 2 (5.7%)             | 0                                                     | 0.173   |
| Chronic constipation                 | 3 (8.6%)             | 3 (9.4%)                                              | 0.910   |
| Gluteal pain                         | 6 (17.1%)            | 7 (21.9%)                                             | 0.631   |
| Chronic constipation + abdominal pain| 4 (11.4%)            | 2 (6.2%)                                              | 0.466   |
| Urinary incontinence                | 0                    | 1 (3.1%)                                              | 0.299   |
| Prolapsed vaginal vault + dyspareunia| 1 (2.9%)             | 0                                                     | 0.343   |
| Abdominal pain + dyspareunia         | 1 (2.9%)             | 1 (3.1%)                                              | 0.950   |
| Vaginal vault dehiscence and eversion| 0                    | 1 (3.1%)                                              | 0.296   |

Fischer’s Exact test was used for categorical variables. P values: P values indicate comparison of 1 year follow-up anatomic outcomes and symptoms between vaginal hysterectomy group and vaginal hysterectomy + sacrospinous ligament fixation group. P<0.05 was considered statistically significant.
vaginal operations because of surgical positioning. Moreover, healing might be quite slow with such damage\(^{(14)}\).

In the present study, there was no significant difference between the two groups in terms of patient satisfaction with their operations. In agreement with the literature, SLF following vaginal hysterectomy did not cause additional symptoms and dissatisfaction in the patients compared with vaginal hysterectomy alone\(^{(15)}\). Furthermore, recurrence of vaginal vault prolapse was significantly more frequent in the VH group compared with the VH+SLF group. However, there was no significant difference between the two groups in cystocele and rectocele recurrence. Previous studies reported that the risk of cystocele recurrence increased in unilateral patients undergoing SLF, not that of apical prolapse\(^{(16-18)}\). In a study in which patients with POP underwent SLF and followed up at one and seven years, the objective cure rate for apical vaginal vault prolapse at 1 and 7 years was 96% (49/51) and 94.28% (33/35), respectively\(^{(19)}\). In the present study, of all the patients with vault prolapse at 1 and 7 years was 96% (49/51) and 94.28% (33/35), respectively\(^{(19)}\). In the present study, 7 (21.9%) patients had gluteal pain, 3 (9.4%) had chronic constipation, and 1 (3.1%) had urinary incontinence as revealed by the 1-year follow-up. In addition, 1 patient (3.1%) had vaginal vault dehiscence and evisceration. There was no significant difference between the groups in 1-year complications. The patient who had intestinal dehiscence underwent vaginal vault repair under local anesthesia.

In their study, Given et al.\(^{(27)}\) suggested that the vagina became shorter after SLF, which possibly caused dyspareunia. In a previous study, the authors indicated an association between dyspareunia and posterior colporrhaphy and prenioplasty in patients who underwent SLF\(^{(28)}\). Lopes et al.\(^{(29)}\) compared mesh with SLF and found that sexual dysfunction was significantly more likely in the mesh group. In the present study, there was no significant difference between the two groups in sexual dysfunction. In addition, no isolated dyspareunia was observed in the VH+SLF group. However, 1 patient (3.1%) in this group reported dyspareunia accompanied by abdominal pain. In this respect, there was no significant difference between the groups in experience of dyspareunia. These results might be explained by the small sample size of the study because only 18 patients (51.4%) in the VH group and 14 (43.8%) in the VH+SLF group were sexually active.

The mean length of operation was 99.2±29.6 min in the VH+SLF group, which is relatively short compared with similar studies in the literature. In addition, the length of operation was significantly longer in the VH+SLF group compared with the VH group. The relatively short mean length of operation may be because the surgeons of Dicle University Hospital, which serves as a tertiary care center, have considerable surgical experience with stage 3 and 4 POP because this condition is quite widespread among women of the region who are very much involved in agricultural activities. On the other hand, length of hospital stay was 3.9±2.5 days in the VH+SLF group, which was significantly higher than that in the VH group. Similar studies in the literature reported shorter length of hospital stay\(^{(30)}\). This result may be explained by the fact that all of the study participants were postmenopausal elderly patients.

Anterior pelvic plane meshes are recommended to secured to the sacrospinous ligament safely during the SLF operation\(^{(31)}\). Mesh was not used in any of our patients.

In conclusion, vaginal hysterectomy with SLF increases the length of operation and hospital stay as well as the risk of
intraoperative and early complications in patients with stage 3 or 4 POP. However, recurrence of vaginal vault prolapse was significantly more frequent after vaginal hysterectomy alone. Given all these, unilateral SLF may be added to vaginal hysterectomy in patients with stage 3 or 4 POP who are predicted to have long survival times. However, further studies with a larger sample sizes are needed in this area of research.

Ethics Committee Approval: The study were approved by the Dicle University of Local Ethics Committee. Informed Consent: Consent form was filled out by all participants. Concept: Elif Ağaçayak, Senem Yaman Tunç, Fatih Mehmet Fındık, Design: Elif Ağaçayak, Sibel Sak, Data Collection or Processing: Yasemin Ceter, Gamze Akın, Analysis or Interpretation: Elif Ağaçayak, Talip Gül, Literature Search: Elif Ağaçayak, Mehmet Sait İçen, Serdar Başaranoğlu, Writing: Elif Ağaçayak, Peer-review: Externally peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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