ORIGINAL RESEARCH
Functional

Doi: 10.4274/jus.galenos.2023.2022.0051
J Urol Surg, 2023;10(3):213-219

Nocturnal Vaginal pH Monitoring: A Possible New Assessment Method for Female Sexual Function

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What's known on the subject? and What does the study add?

Male sexual arousal response is penile erection due to vasocongestion. There is also a phenomenon that men have 4 or more penile erection phases lasting at least 30 min during night sleep. In females, sexual arousal responses are clitoral engorgement and vaginal lubrication. These responses are also seen due to vasocongestion. It is unknown whether females have similar nocturnal vasocongestion episodes. This study investigated whether women have nocturnal vasocongestion episodes like men and whether nocturnal vaginal pH monitoring can be used for female sexual function assessment such as nocturnal penile tumescence and rigidity test in men.

Abstract

Objective: The aim of this preliminary study was to investigate whether women have nocturnal vasocongestion episodes like men and whether nocturnal vaginal pH (NVpH) monitoring can be used for female sexual function assessment-like nocturnal penile tumescence and rigidity (NPTR) test in men.

Materials and Methods: Twelve premenopausal volunteers were included in the study. All women were within sexually active age and had normal hormonal profiles. NVpH was performed in an ambulatory manner on the same day and phase of the menstrual cycle. Female sexual function index (FSFI) scores, lubrication scores, and clitoral artery peak systolic velocity (PSV) were recorded. The volunteers were grouped according to the number of elevated pH episodes (EPE).

Results: Four women had four or more EPEs and constituted group 1. Eight women had 3 or less EPEs and constituted group 2. Group 2 had statistically significantly lower FSFI scores and clitoral artery PSV (p=0.001 and p=0.014, respectively). However, there was no statistically significant difference between the groups for lubrication scores and age.

Conclusion: The results of this preliminary study suggested that women and men has the same nocturnal vasocongestion episodes and NVpH measurement in women might be considered as analogous to NPTR in men.

Keywords: Femal, hydrogen-ion concentration, physiologica, sexual function, the vagina

Introduction

Sexual complaints are reported by approximately 40% of women worldwide (1,2). The most reported types of dysfunction are low sexual desire (26 to 43%) and inability to reach orgasm (18 to 41%) (1). Self-reports by women often do not distinguish between desire and arousal (3). Arousal may be either subjective (thoughts, feelings) or objective (genital vasocongestion or lubrication) (3). The management of difficulty with arousal must be tailored to whether the problem is subjective, objective, or combined.

Male sexual arousal response is penile erection due to vasocongestion. There is also a phenomenon that men have 4 or more penile erection phases lasting at least 30 min during night sleep, and analogous phenomena are present in women (4,5).

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Received: 16.05.2022 **Accepted:** 15.01.2023

Cite this article as: Gören MR, Özer C, Oğuzülgen İ. Nocturnal Vaginal pH Monitoring: A Possible New Assessment Method for Female Sexual Function. J Urol Surg, 2023;10(3):213-219.

In females, sexual arousal responses are clitoral engorgement and vaginal lubrication (6). These responses are also seen due to vasocongestion (7). It is unknown whether females have similar nocturnal vasocongestion episodes.

The female sexual response cycle includes four phases: desire (libido), arousal (excitement), orgasm and resolution. The arousal phase entails a subjective sense of sexual pleasure accompanied by physiologic changes, including genital vasocongestion and increase in heart rate, blood pressure, and respiratory rate (8). Within the sexually aroused vagina, the capillaries of the microcirculation are filled with blood, causing an increase in hydrostatic pressure inside them that forces out a plasma transudate (ultrafiltrate) into the interstitial space around the blood vessels (9). This increases the resting vaginal pH. The normal value of vaginal pH for premenopausal women is ≤4.5 (10,11).

The sexual physiology of males and females are similar. The sexual dysfunction in women and men can be due to organic or psychological factors. Male sexual dysfunction can be diagnosed with several quantitative tests such as the (NPTR) test, penile colored Doppler ultrasonography, and others, whereas the quantitative assessments of female sexual dysfunction are limited. In the past, many studies were performed to understand the female sexual function (FSF) using different methods including genital blood flow measurement, vaginal photoplethysmography (VP), vaginal and labial thermistors, thermography, clitoral and labial photoplethysmography, duplex Doppler ultrasonography and laser Doppler perfusion imaging of the female genitalia, dynamic contrast and non-contrast magnetic resonance imaging, laser oximetry, clitoral intracavernosal pressure, pudendal arteriogram and vaginal pH measurement (12). However, most of these methods are considered experimental except VP. Additionally, the common feature of these methods is that they require clinical and technical experience.

Knowledge and experience of the male sexual dysfunction are more settled; therefore, application of this knowledge to female sexual dysfunction might lower the workload needed to design diagnostic tests for FSD. The aim of this preliminary study was to investigate whether women have nocturnal vasocongestion episodes like men and whether nocturnal vaginal pH monitoring can be used for female sexual function assessment the NPTR test in men.

Materials and Methods

The study protocol was approved by the Institutional Review Board and Ethics Committee of Başkent University (project no: KA06/143, date: 07.06.2006).

Volunteers

Healthy sexually active premenopausal unpregnant women whom defining themselves as sexually normal and healthy were included in the study. Women with a history of vaginal/pelvic surgery, radiotherapy, or infection, and those taking any medications, including oral contraceptives were excluded. All volunteers were evaluated with validated Female Sexual Function Index (FSFI) scores, genital examination, and hormonal profile, including serum thyroid-stimulating hormone, follicle stimulating hormone, luteinizing hormone, prolactin, testosterone, and estradiol (13,14). Twelve women were enrolled in the study. All volunteers' hormonal profiles were within normal limits. The vaginal cultures did not indicate infection before pH monitoring. Informed consent was obtained from all individual participants included in the study. All volunteers' menstrual cycle lengths were recorded. Before every pH measurement, procedure volunteers were evaluated with vaginal culture and β-human chorionic gonadotropin serum level to prove the absence of vaginal infection and pregnancy, which may affect vaginal pH, respectively. All volunteers' lubrication scores were calculated according to FSFI questionaries' questions 7, 8, 9, and 10.

Ambulatory pH Monitoring

Nocturnal pH monitoring was performed in an ambulatory manner using an Orion II™ recording device [Medical Measurements Systems (MMS), Enschede, The Netherlands USA] and single crystal antimony pH catheters (Synectics Medical, Sweden) (Figure 1). This device is commonly used for diagnosis of gastroesophageal reflux. All measurements were done at the volunteers' home. The catheters were calibrated with solutions having pH 1 and 7 before each recording. All volunteers were educated for the placement and fixation of the catheter and for the operating procedures of Orion II. The pH catheters were marked with a water-resistant marker from 7 cm of the tip. The volunteers placed the pH catheters inside their vagina till to marker on the catheter just before night sleep. The mark on the pH catheters guaranteed as the active point of the catheter

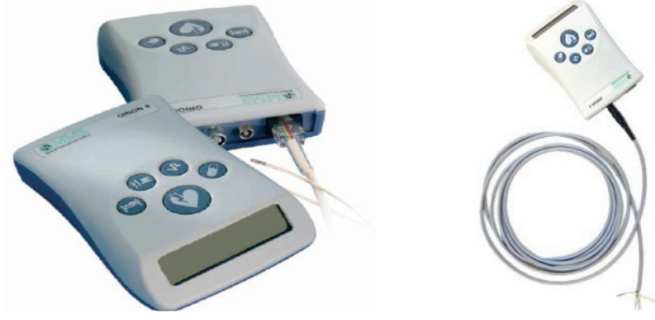

Figure 1. Orion II™ ambulatory pH recorder (Medical Measurements System, Enschede The Netherlands)

would be approximately 5 cm from the introitus. The catheters were fixed to the labium magus with a medical plaster to keep them in place during one-night sleep. The catheter is also fixed by three medical plaster locations to the leg. The volunteers kept the Orion II device at the top of the chiffonier beside the bed to be undisturbed due to the device. To minimize the hormonal effects, all volunteers were asked to use the device 10 days before menstruation. All measurements were done at least twice. The repeating measurements were performed in the following menstrual cycle. The recorded data were evaluated for mis-recordings such as dislocation of the catheter, halting of recording due to finished battery, or gross movements (such as walk to urination, awakening etc.). In the case of mis-recording, the procedure was repeated in the following menstrual cycle.

Clitoral Artery Peak Systolic Velocity Measurements

Clitoral colored Doppler ultrasonography was performed with a 7.5 MHz linear transducer (Acuson, Siemens, Germany). The ultrasound probe was applied sagittally proximal to the clitoris root, as described in previous reports (15,16). Bilateral clitoral cavernosal artery diameter and peak systolic velocity (PSV) parameters were recorded. A clitoral artery PSV ≥10 cm/s was accepted as normal (15).

Data Evaluation

A chart of the nocturnal vaginal pH values was plotted using the recording device's computer-based software (MMS, The Netherlands). All recordings were evaluated for mis-recordings. The mis-recordings were detected seen in the pH charts as unexpected pH changes as seen in before sleep part of the Figure 1A. The last successful set of recordings were evaluated. A pH elevation greater than 6, lasting for more than 30 minutes, was considered an elevated pH episode (EPE) that was an indicator of vasocongestion episode. Four or more EPEs were accepted as an indicator of normal FSF. Three or less EPEs were considered an indicator of inadequate FSF. The volunteers were divided into 2 groups according to sexual function based on the number of EPEs; group 1 consisted of the volunteers with 4 or more EPEs, and group 2 consisted of the volunteers with 3 or less EPEs.

Statistical Analysis

Statistical analyses were performed using the statistical package SPSS (Version 23.0; IBM SPSS Inc., Chicago, IL, USA). For each continuous variable, normality was checked by the Kolmogorov-Smirnov's test, Shapiro-Wilk's test, and histograms. Welch's t-test was used for the comparison between groups and $p<0.05$ was considered as statistically significant (17). A post-hoc power analysis for t-test is performed.

Results

The mean age of the volunteers was 32.4±4.9 (range; 25-41) years. None of the recorded pH values was below 4, and the maximum-recorded value was 6.2. The FSFI scores of the volunteers ranged between 7.8 and 28.6 (median; 16.55), and the lubrication scores ranged between 0.9 and 6 (median; 3.9). The clitoral artery PSV ranged between 4 to 15 cm/s (median; 10 cm/s). The recorded EPEs were ranged between 0 and 5 (median; 2). The FSFI and lubrication scores of the volunteers according to age and clitoral PSV values and min/max NVpH levels are summarized in Table 1.

Four women had 4 or more nocturnal EPEs, and 8 women had 3 or less nocturnal EPEs. Group 1 consisted of 4 women and group 2 consisted of 8 women. Group 2 had significantly lower FSFI scores and clitoral artery PSV (p=0.001 and p=0.014,

Table 1. The Female Sexual Function index, lubrication scores, clitoral artery peak systolic velocity values, and number of elevated pH episodes of the volunteers

Volunteer number	Age (years)	FSFI[a]	Lubrication score	Clitoral PSV[b] (cm/s)	Number of EPE[c]	Min-max pH
1	25	15.40	3.3	6.00	1	4.48-6.02
2	26	7.80	0.9	9.00	0	5.36-5.66
3	28	21.30	5.1	14.00	4	4.27-6.20
4	30	26.90	4.8	15.00	4	4.01-6.15
5	31	28.60	5.1	11.00	5	4.49-6.19
6	32	11.50	3.0	4.00	0	5.36-5.68
7	32	25.90	2.1	12.00	4	4.89-6.11
8	33	9.40	0.9	10.00	0	4.21-5.76
9	35	21.80	6.0	8.00	3	4.68-6.07
10	36	13.10	5.7	10.00	0	4.10-5.17
11	40	17.70	4.2	15.00	2	5.01-6.08
12	41	14.10	3.6	6.00	2	4.51-6.06

[a]FSFI: Female Sexual Function index, [b]Lubrication score: Calculated with questions 7, 8, 9, and 10 of the FSFI Questionnaire, PSV: Peak systolic velocity of the clitoral artery, [c]EPE: Elevated pH episode

respectively) (Table 2). There was no statistically significant difference in lubrication scores and age between both groups (Table 2). The post-hoc power analysis of the study was 0.998.

The nocturnal pH charts of the volunteers with FSFI scores 26.9 and 9.4 are shown and compared with the nocturnal penile tumescence charts in Figure 2.

Discussion

Female sexual dysfunction is a multi-causal and multidimensional medical problem that has both biological and psychosocial components (18). The multidimensional nature of FSD mandates an understanding of the normal physiology of FSF. One of the easiest methods for the assessment of FSF is scoring questionnaires (13,14). FSFI is widely accepted and used for assessing FSF. An FSFI score ≤26.55 is associated with FSD (19). However, FSD can be diagnosed according to the current Diagnostic and Statistical Manual of Mental Disorders (8). Assesses 6 subheadings such as desire, arousal, lubrication, orgasm, satisfaction, and pain; therefore, the score does not identify the underlying pathology as organic or psychological. In this study, we used the FSFI scores to identify the volunteers' sexual function status and the volunteers' FSFI scores ranged between 7.8 and 28.6. Only 2 of the volunteers' FSFI scores were

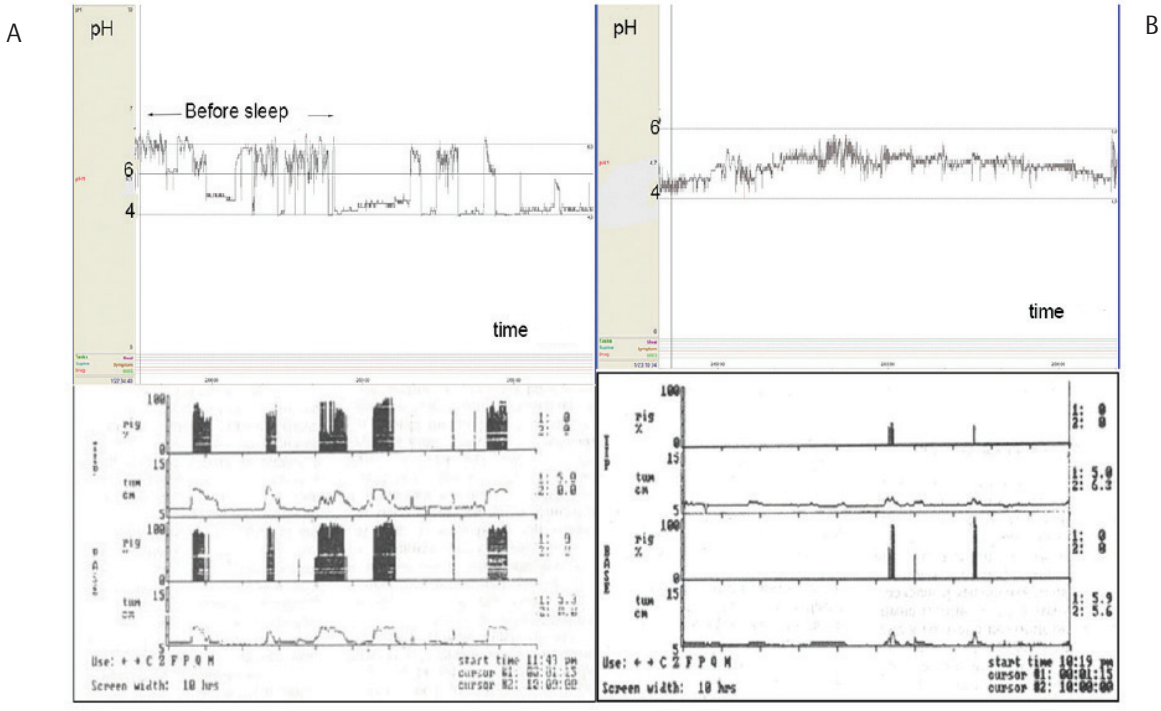

Figure 2. Comparison of nocturnal pH monitoring charts with nocturnal penile tumescence and rigidity (NPTR) charts

A. Nocturnal pH chart of a 30-year-old female volunteer with a FSFI score 26.90. Her chart was compared with a non-pathologic NPTR chart. On the right section of the chart, 3 of 4 elevated pH episodes can be seen. Each episode lasted more than 30 min. The pH fluctuations before sleep were caused due to gross movements

B. Nocturnal pH chart of a 33-year-old female volunteer with a FSFI score 9.40. Her chart is compared with a non-erected NPTR. There was no increased vaginal pH episodes during nocturnal monitoring

FSFI: Female Sexual Function index, NPTR: Nocturnal penile tumescence and rigidity

Table 2. Comparison between the two groups

	Group 1 (number of EPE ≥4) (n=4) Median (min-max)	Group 2 (number of EPE<4) (n=8) Median (min-max)	p-value
Age	30.5 (28-32)	34 (25-41)	0.179
FSFI[a]	26.4 (21.3-28.6)	13.6 (7.8-21.8)	0.001
LS[b]	4.95 (2.1-5.1)	3.45 (0.9-6)	0.430
PSV[c]	13 (11-15)	8.5 (4-15)	0.014

[a]FSFI: Female Sexual Function index, [b]LS: Lubrication score, calculated with questions 7, 8, 9, and 10 of the FSFI Questionnaire, [c]PSV: Peak systolic velocity of the clitoral artery ,EPE: Elevated pH episode

above 26.55. This was an unexpectedly high rate of low FSFI scores in the absence of organic or psychological problems. This might be explained by volunteer bias.

In 1968, Shapiro et al. (20) performed the first studies to assess vaginal acidity. They could not show the alteration of pH with the technology available at that time. With the improvement in the pH measurement technology, Masters and Johnson reported that vaginal pH increased slightly with sexual arousal. However, continuous measurement of vaginal pH with radiotelemetry during sexual intercourse revealed that vaginal lubrication did not appreciably change the pH (12). Nevertheless, this report was based on the results from two couples only. Wagner and Levin investigated the surface pH of the vagina before and after sexual arousal by self-stimulation and found that clitoral self-stimulation to orgasm generally results in a small increase in pH by up to 1 unit (12). Berman et al. (21) used a digital pH-meter inserted into the vagina and found an increase in pH post self-stimulation and with sildenafil, and they also reported an increase in baseline mean vaginal pH measurements to 6 following sexual stimulation. In our study, the nocturnal vaginal pH of the volunteers ranged between 4 and 6.2, and elevated pH over 6 lasting more than 30 min was considered an indicator of vasocongestion episode. The pH elevations over the threshold, 6, can be considered as ignorable. However, pH is calculated as $-\log[H^+]$; thus, the hydrogen ion concentration change for every pH unit is not equal.

All NVpH measurements were performed 10 days before the menstruation. This day was decided using three parameters. The menstrual cycle has four phases such as follicular, ovulation, luteal and menstruation. The sexual arousal of women changes within these phases (22). It has been shown that sexual arousal peaks with ovulation and remains high till the mid-luteal phase (22). The mid-luteal phase starts one week after the ovulation. The vaginal pH, salivary pH, and body temperature are changed during ovulation (23). To the best of our knowledge, there is no confirmed vaginal pH-level changes in the luteal phase. The luteal phase duration is almost the same in healthy women therefore it is easy to calculate the mid-luteal phase (24). The day, which NVpH measurements were done has the beneficial effects such as high sexual arousal and avoiding pH-level changes in ovulation.

The glandulae vestibulares majores (larger vestibular or Bartholin glands) actively secretes clear, viscid, and stringy mucoid substance with an alkaline pH during sexual activity (11). Vaginal lubrication can be considered to be the keystone of pH alteration during sexual arousal. Thus, in this study, the lubrication scores were separately evaluated, but there was no statistically significant difference in the lubrication scores between both groups. There was an interesting finding in the pH charts. The pH elevation during EPEs can be explained with the alkaline secretions, but the pH sharply decreased to basal levels at the end of the EPEs. The pH catheter used in this study has only one active point. The alkaline secretions are moving toward the labium magnus; thus, when the alkaline fluid passed the active point of the catheter, it measures the acidic vaginal mucosa pH (25).

Vaginal photoplethysmography has been the most widely used physiological measurement of vaginal vasocongestion, demonstrating adequate validity and reliability in psychophysiological studies of healthy and sexually dysfunctional women. Several other physiological measurement approaches have been proposed and are in development, including measurements of clitoral and labial temperature and oxygenation, vaginal and clitoral Doppler, and blood flow measurements and vaginometry. Despite the obvious interest and appeal of these alternatives, none has been adequately validated or standardized in patients or healthy controls (26). Vaginal pulse amplitude (VPA) and vaginal blood volume can be calculated using VP (27). Vaginal photoplethysmography requires special equipment that can cost more than $10,000; thus, it is a relatively expensive technique (27). In summary, the measurement of VPA with VP are laboratory-based methods to provide specific information about the impact of various conditions on vaginal blood flow. Although VP is considered to be the most reliable method for assessing vaginal blood flow, it has limitations such as potential bias and high cost (27). Nocturnal vaginal pH monitoring can be done at home; it is cheaper than VP and might reduce the potential bias.

Men and women have similar sexual physiology with different promoters. Therefore, the implementation of the concepts behind male sexual dysfunction diagnostic techniques to women might be possible with experience and after standardization. Clitoral artery PSV measurement is equivalent to penile cavernosal artery PSV measurement. The normal values of basal clitoral artery PSV are not yet been standardized, therefore in our study, clitoral PSV was not used as the primary diagnostic criterion for FSD. However, duplex Doppler ultrasound studies in women with sexual dysfunction were useful in a diagnostic and therapeutic contexts (28). In this study, clitoral artery PSV ≥10 cm/s was accepted as normal, according to previous reports (15,16). However, group 2 had significantly lower clitoral artery PSV than group 1, which also supported the feasibility of nocturnal vaginal pH monitoring on evaluation of FSF.

The NPTR monitoring reflects the integrity of the efferent arm of the erectile reflex, indirectly testing the neural, vascular, and hormonal influences on erectile function. Many clinicians use NPTR testing as the noninvasive reference standard for the differentiation between organic and psychogenic causes of erectile dysfunction (29). In men, sleep-related erections are present throughout life with only a slight decline in older

healthy people, and analogous phenomena are present in women (5). The recommended criteria for normal NPTR include 4-5 erectile episodes per night with a mean duration longer than 30 min, and an increase in the circumference of more than 3 cm at the base and more than 2 cm at the tip, with a maximal rigidity above 70% at both the base and tip (30). In males, both sexual arousal response and nocturnal penile erection are due to vasocongestion (4,31). In females, the sexual arousal response is clitoral erection and lubrication due to vasocongestion (6). In males, if 4 or more nocturnal vasocongestion episodes, which represent as penile erection, are normal, females might have the same physiology. Therefore, in this study, we considered 4 or more EPEs as an indicator of normal female sexual function. Four women with an FSFI score ≥21.8 had 4 or more EPEs. However, 4 women with an FSFI score <13.1 did not have EPE. Four women with an FSFI scores between 14.1 and 21.8 had between 1 and 3 EPEs. In our study, nocturnal vaginal pH peaks in women with FSFI score ≥21.8 revealed similar characteristics as NPTR as seen in Figure 1. In Figure 1, the woman with an FSFI score 26.9 had 4 EPEs (3 of 4 are shown in the Figure), and the chart of these pH episodes was very similar to the model NPTR chart. In our study, all women-except that one with FSFI score ≥21.8-had ≥4 EPEs. A volunteer with an FSFI score of 25.9 had 3 EPEs.

Study Limitations

There were 3 limitations of this study. The main limitation was the number of women involved in the study. Therefore, the data were analyzed with the Welch's t-test because the sample size was small (less than 10) and unequal (17). Despite the use of post hoc power analysis controversial, we have performed post hoc power analysis to define the interpretability of our data, and the result of the analysis was 0.998. Although the number of volunteers was limited, the data obtained from this study revealed important results.

Second, the electrodes used in this study were made of antimony. Antimony electrodes are affected by the oxygen tension of the fluids (32). This might have altered the vaginal pH measurements. However, the electrode was calibrated before all the measurements. Finally, this was a volunteer-based study; therefore, volunteer bias is expected.

Our data must be confirmed with studies including healthy and sexually dysfunctional women and men. These studies should evaluate sleep cycles with electroencephalography and evaluate vaginal blood flow with photoplethysmography and assess sexual function with different questionnaires in women.

Conclusion

Women and men might have the same nocturnal vasocongestion episodes, and NVpH measurement in women might be considered as analogous to NPTR in men. More studies on larger populations, including healthy subjects and patients with FSD, are required to define this technique and to make a better comment on the results.

Ethics

Ethics Committee Approval: The study protocol was approved by The Başkent University's Institutional Review Board and Ethics Committee (project no: KA06/143, date: 07.06.2006).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Concept: M.R.G, İ.O., Design: M.R.G, C.Ö., Data Collection of Processing: M.R.G, İ.O., Analysis or Interpretation: M.R.G, C.Ö., İ.O., Literature Search: M.R.G., Writing: M.R.G., C.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

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