

The Effects of Lens Extraction Surgery on Intraocular Pressure and Anterior Segment Parameters in Primary Angle-Closure Glaucoma

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Abstract

Objectives: To investigate the effects of phacoemulsification with intraocular lens implantation (phaco+IOL) surgery on intraocular pressure (IOP) and anterior segment parameters in patients with cataract and primary angle-closure glaucoma (PACG).

Materials and Methods: Fifty-five patients with PACG undergoing phaco+IOL surgery were evaluated in terms of best corrected visual acuity (BCVA), IOP, anterior chamber depth (ACD), aqueous depth (AD), and lens thickness (LT) measured by optical biometry preoperatively and at the 6-month postoperative visit. They were compared with 34 healthy ageand gender-matched cataract patients who underwent phaco+IOL surgery.

Results: Preoperative evaluation revealed higher IOP, shorter axial length, shallower ACD and AD, and greater LT in the PACG group (p<0.001 for all). Postoperative evaluation in the PACG group showed an increase in BCVA, a significant decrease in IOP, an increase in ACD and AD, and a decrease in LT (p<0.001 for all). Additionally, a reduction in the average number of antiglaucomatous medications used postoperatively was observed in the PACG group (p<0.001). The changes in IOP, ACD, AD, and LT between preoperative and postoperative assessments were significantly greater in the PACG group compared to the control group (p<0.0001 for all).

Conclusion: Phaco+IOL surgery in PACG patients leads to a significant increase in ACD compared to the control group and allows better control of IOP with fewer antiglaucomatous medications after surgery.

Keywords: Primary angle-closure glaucoma, lens extraction, intraocular pressure, anterior segment parameters

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Introduction

Glaucoma is a progressive optic neuropathy characterized by damage to retinal ganglion cells and their axons.¹ Early diagnosis and treatment of glaucoma, which is one of the leading causes of irreversible blindness worldwide, are crucial in preventing vision loss.^{1,2} Primary angle-closure glaucoma (PACG), an important subtype of glaucoma, is less common than primary open-angle glaucoma (POAG) but tends to have a more aggressive course.^{2,3} PACG affects around 20 million people globally, particularly in East Asia.³ It is estimated that this number will exceed 34 million by the year 2040, with an estimated risk of blindness for 5.3 million people.³ While most patients do not experience complete vision loss, their quality of life is reduced by peripheral visual field narrowing and the need for long-term treatment.²

Angle closure occurs due to anatomical features that lead to the narrowing or closure of the iridocorneal angle.^{4,5} This closure can occur through either synechial or appositional mechanisms, both of which obstruct the flow of aqueous humor. PACG is defined as the presence of glaucomatous optic nerve damage with more than 180° of the iridocorneal angle blocked due to apposition between the iris and the trabecular meshwork, accompanied by elevated intraocular pressure (IOP).⁴

It is known that various factors, including an increase in lens thickness (LT) or curvature, narrow anterior chamber depth (ACD), hyperopic eyes, zonular dialysis leading to anterior displacement of the lens, pupillary block triggered by the lens, and iris configuration play important roles in the pathogenesis of PACG.^{2,4,5,6,7,8}

In the treatment of PACG, the traditional method known as laser peripheral iridotomy (LPI) is effective in preventing acute angle-closure attacks. However, it may not open the angle in up to 58% of eyes with PACG.⁴ Phacoemulsification with intraocular lens implantation (phaco+IOL) surgery not only enhances visual acuity but also effectively lowers IOP, diminishes reliance on antiglaucoma medications, and can potentially

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decrease the necessity for subsequent glaucoma surgeries in these patients.^{1,2,5,6,7,9} Compared to LPI, initial phaco+IOL is 10 times more likely to help patients with PACG maintain good IOP control without the need for antiglaucomatous medication.9 Furthermore, lens extraction can correct the commonly encountered hyperopic refractive error in these patients, reducing the need for glasses or contact lenses and improving their quality of life.10 In recent years, the Effectiveness of Early Lens Extraction for the treatment of primary angle closure glaucoma (EAGLE) study also evaluated clear lens extraction (CLE) surgery in PACG patients without cataract.^{2,9} However, the potential risks of complications associated with phaco+IOL surgery in PACG patients should not be disregarded.^{2,5,6,7} This is because these eves have risk factors such as elevated IOP, decreased endothelial cell count and function, narrow anterior chamber space, floppy iris due to previous iris ischemia, posterior synechiae, increased LT, and loose lens zonules.^{2,4,6,11,12} These factors increase the difficulty of intra- and postoperative management, and inexperienced surgeons performing lens surgery in such eyes can lead to potentially devastating complications such as posterior capsule rupture, lens drop, suprachoroidal hemorrhage and potential complications such as malignant glaucoma.^{2,4,12}

The present study aims to investigate the visual outcomes, changes in IOP, and the need for postoperative antiglaucoma treatment in PACG patients undergoing phaco+IOL surgery for cataract. Additionally, the differences in preoperative and postoperative anterior segment parameters were compared between the PACG group and a control group consisting of patients with no condition other than cataract who underwent phaco+IOL surgery.

Materials and Methods

This prospective cross-sectional study was conducted in the glaucoma unit of a tertiary referral eye hospital. Fifty-five eyes of 55 patients who received medical treatment for PACG and underwent phaco+IOL surgery for cataract were compared to a control group consisting of 34 eyes of 34 age- and gendermatched patients with no health conditions other than cataract who also underwent phaco+IOL surgery. All participants were provided with detailed information about the nature of the study and their written informed consent was obtained. The study protocol was approved by the Ankara Training and Research Hospital Ethics Committee (number: 15.09.2021 E-21/661). All study procedures were planned in accordance with the ethical principles of the Helsinki Declaration and Good Clinical Practice Guidelines.

A thorough ophthalmological examination was performed on all participants after obtaining a detailed ocular and systemic medical history. This examination included best-corrected visual acuity (BCVA) with Snellen chart, IOP measurement with Goldmann applanation tonometry, gonioscopy with a Goldmann three-mirror lens, slit-lamp biomicroscopy of the anterior segment and fundus examination, visual field assessment using the Humphrey Visual Field Analyzer with the standard 24-2 Swedish Interactive Threshold Algorithm strategy, and measurement of anterior segment parameters including central corneal thickness (μ m), ACD (mm), aqueous depth (AD) (mm), and LT (mm) using the Lenstar 900 optical biometry device (Haag-Streit AG, Koeniz, Switzerland). Within the scope of the study, all measurements were obtained both before cataract surgery and at the 6-month postoperative visit.

The diagnosis of PACG was made according to the criteria of the European Glaucoma Society Guidelines.¹³ The criteria for the diagnosis of PACG included untreated IOP >21 mmHg, iridotrabecular contact of 180° or more on gonioscopy (peripheral iris pushed forward and in appositional or synechial contact with Schwalbe's line), glaucomatous appearance of the optic nerve head (e.g., neuroretinal rim thinning, notching, cup-to-disc ratio asymmetry, focal hemorrhages), and the presence of glaucomatous visual field defects. Patients with primary angle closure without glaucomatous findings and primary angle closure suspects were excluded from the study.

Participants with nuclear lens opacities higher than grade 2 were included in the study with the dual aim of enhancing visual quality by addressing cataracts that reduce vision and providing more effective glaucoma control in the PACG group after cataract surgery. All participants in the PACG group had a patent LPI prior to phaco+IOL surgery. All surgical procedures were performed by the same experienced surgeon (E.Ş.) using the same device (Centurion Systems Alcon Surgical, Fort Worth, Texas, USA) and similar torsional phaco, vacuum, and aspiration flow parameters. In all surgeries, an Alcon SA60AT single-piece, aspheric, hydrophobic acrylic, monofocal, foldable IOL (Alcon Laboratories, Inc.) was implanted according to the measurements obtained from Lenstar 900 (Haag-Streit AG, Koeniz, Switzerland) optical biometry, and 0.1 mL/1 mg of intracameral cefuroxime (Aprokam, Thea Pharma İlaç, İstanbul, Türkiye) was administered at the end of the surgery. No complications occurred during or after the surgeries. An anterior chamber biomicroscopy image of a patient from the PACG group before and after surgery can be seen in Figure 1.

Participants with a history of glaucoma other than PACG, non-glaucomatous optic neuropathy, previous ocular surgery, trauma or laser procedures, vitreoretinal diseases (e.g., such as diabetic retinopathy, hypertensive retinopathy, retinal vascular occlusions), active intraocular infections or inflammation, eyes with intraocular conditions that may affect anterior segment findings (e.g., corneal scars, pseudoexfoliation, uveitis), over 3D of myopia, hyperopia, or astigmatism, and patients diagnosed with systemic diseases (e.g., diabetes mellitus, arterial hypertension, coronary artery disease, history of malignancy) were excluded. Additionally, patients who did not attend regular follow-up or could not cooperate with the measurements were also excluded from the study.

Statistical Analysis

The statistical analyses were conducted using IBM[®] SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The normality of continuous variables was examined using the

Kolmogorov-Smirnov test. Comparisons between the study groups was performed using the independent-samples t-test. The paired-samples t-test was used to compare preoperative and postoperative findings within the groups. The presence of correlation between numerical variables was evaluated using



Figure 1. An anterior chamber biomicroscopy image of a patient from the primary angle-closure glaucoma group before (A, C) and after surgery (B, D). The anterior chamber depth in the slit-lamp biomicroscopic image is shallow before (C) and deep after surgery (D)

the Pearson correlation test. A significance level of 0.05 was established for statistical significance.

Results

There was no significant difference in demographic data between the PACG group and the control group (Table 1). Before surgery, BCVA was better in the control group, while the PACG group had significantly higher IOP and LT values and significantly lower AL, AD, and ACD values than the control group (p<0.001 for all). There was no significant difference in central corneal thickness between the two groups (p=0.05). The preoperative BCVA, IOP, and anterior segment parameters of the study groups are summarized in <u>Table 1</u>, and the postoperative findings are presented in <u>Table 2</u>.

After surgery, the PACG group showed a significant decrease in IOP, an increase in ACD and AD, and a decrease in LT (p<0.001 for all). Additionally, the number of antiglaucoma eye drops used significantly decreased compared to the preoperative period (p<0.001). The preoperative and postoperative findings of the PACG group are compared in <u>Table 3</u>.

When compared to the control group, the PACG group showed statistically significantly greater changes in IOP, ACD, AD, and LT between the pre- and postoperative measurements (p<0.0001 for all) (Table 4).

| of the study groups | | | | | |
|---|----------------------------------|-------------------------------------|----------------|--|--|
| | PACG (n=55) Mean ± SD (range) | Control (n=34) Mean ± SD (range) | p ^a | | |
| Age (years) | 63.7±10.7 (36-83) | 61.4±9.9 (40-82) | 0.31 | | |
| Best corrected visual acuity (Snellen decimal) | 0.45±0.30 (0.05-0.8) | 0.14±0.12 (0.05-0.5) | <0.001 | | |
| Intraocular pressure (mmHg) | 20.1±6.41 (10-30) | 15.5±3.39 (9-21) | <0.001 | | |
| Axial length (mm) | 22.08±0.7 (20.61-23.27) | 23.60±0.9 (21.77-24.79) | <0.001 | | |
| Central corneal thickness (µm) | 539.8±38.2 (449-619) | 523.9±33.4 (464-587) | 0.05 | | |
| Aqueous depth (mm) | 1.86±0.16 (1.52-2.38) | 2.78±0.4 (2.08-3.91) | <0.001 | | |
| Anterior chamber depth (mm) | 2.4±0.17 (1.99-2.68) | 3.3±0.37 (2.63-4.06) | <0.001 | | |
| Lens thickness (mm) | 4.86±0.34 (4.20-5.61) | 4.25±0.41 (3.20-4.90) | <0.001 | | |
| Independent samples t test SD: Standard deviation PACC: Primary angle closure alayong | | | | | |

Table 1. Demographic data, preoperative visual acuity, intraocular pressure measurements, and anterior chamber parameters of the study groups

| Table 2. Postoperative visual acuity, intraocular pressure measurements, and anterior chamber parameters of the study groups | | | | | |
|--|----------------------------------|-------------------------------------|----------------|--|--|
| | PACG (n=55) Mean ± SD (range) | Control (n=34) Mean ± SD (range) | P ^a | | |
| Best corrected visual acuity (Snellen decimal) | 0.78±0.19 (0.6-1) | 0.81±0.12 (0.6-1) | 0.27 | | |
| Intraocular pressure (mmHg) | 15.1±2.83 (10-24) | 14.5±3.1 (9-20) | <0.05 | | |
| Axial length (mm) | 22.02±0.7 (20.57-23.20) | 23.5±0.9 (21.69-24.65) | <0.001 | | |
| Central corneal thickness (µm) | 539.7±39.8 (456-627) | 532.1±32.6 (466-590) | 0.35 | | |
| Aqueous depth (mm) | 3.5±0.26 (2.65-4.51) | 4.0±0.31 (3.36-4.82) | <0.001 | | |
| Anterior chamber depth (mm) | 4.02±0.26 (3.24-4.46) | 4.5±0.3 (3.38-5.27) | <0.001 | | |
| Lens thickness (mm) | 0.75±0.02 (0.68-0.80) | 0.68±0.08 (0.52-0.90) | <0.001 | | |
| ^a Independent samples t-test, SD: Standard deviation, PACG: Pri | mary angle-closure glaucoma | | | | |

| Table 3. Comparison of preoperative and postoperative findings in the primary angle-closure glaucoma group | | | | | |
|--|-----------------------------------|------------------------------------|-----------------------|--|--|
| | Preoperative Mean ± SD (range) | Postoperative Mean ± SD (range) | p ^a | | |
| Best corrected visual acuity (Snellen decimal) | 0.45±0.30 (0.05-0.8) | 0.78±0.19 (0.6-1) | <0.001 | | |
| Intraocular pressure (mmHg) | 20.1±6.41 (10-30) | 15.1±2.83 (10-24) | <0.001 | | |
| Aqueous depth (mm) | 1.86±0.16 (1.52-2.38) | 3.5±0.26 (2.65-3.96) | <0.001 | | |
| Anterior chamber depth (mm) | 2.4±0.17 (1.99-2.68) | 4.02±0.26 (3.24-4.46) | <0.001 | | |
| Lens thickness (mm) | 4.86±0.34 (4.20-5.61) | 0.75±0.02 (0.68-0.80) | <0.001 | | |
| Antiglaucomatous medications | 2.9±1.16(1-4) | 1.7±1.2(0-3) | <0.001 | | |
| *Paired samples t-test, SD: Standard deviation | | | | | |

Table 4. Comparison of preoperative and postoperative differences in anterior chamber parameters between the two groups

| | PACG Mean ± SD (range) | Control Mean ± SD (range) | p * | |
|---|---------------------------|------------------------------|------------|--|
| Intraocular pressure (mmHg) | 5.04±6.44 (-3-27) | 0.94±3.03 (-5-8) | <0.0001 | |
| Aqueous depth (mm) | 1.64±0.25 (0.75-2.05) | 1.25±0.30 (0.74-2.36) | <0.0001 | |
| Anterior chamber depth (mm) | 1.62±0.25 (0.79-2.00) | 1.19±0.29 (0.39-1.77) | <0.0001 | |
| Lens thickness (mm) | 4.05±0.45 (1.82-4.89) | 3.6±0.41 (2.52-4.31) | < 0.0001 | |
| *Independent samples t-test, SD: Standard deviation, PACG: Primary angle-closure glaucoma | | | | |

Mean deviation values on the visual field test were -3.43 ± 1.95 decibels (dB) and pattern standard deviation values were 3.06 ± 1.74 dB in the PACG group. Preoperative and postoperative mean gonioscopic grades were 0.64 ± 0.32 (range: 0-1) and 2.04 ± 0.68 (range: 1-3) in the PACG group, and 2.89 ± 0.74 (range: 2-4) and 3.26 ± 0.56 (range: 2-4) in the control group, respectively.

Postoperative IOP reduction was correlated with preoperative AD (r=-0.28, p=0.008) and preoperative ACD (r=-0.27, p=0.009) but not with preoperative LT (r=0.19, p=0.064).

Discussion

The standard treatment for PACG involves LPI to open the aqueous outflow pathway and medical treatment with topical antiglaucoma eye drops to reduce IOP.2,6,7,8 Surgical intervention should be considered for patients who are not adequately controlled with these methods.^{6,7} Phaco+IOL surgery has shown promising results for PACG and can serve as a stand-alone treatment or be performed in combination with the aforementioned modalities.^{5,6,7} Studies comparing phaco+IOL and trabeculectomy surgeries in PACG patients have shown similar long-term IOP control between the methods, with trabeculectomy patients requiring fewer postoperative glaucoma medications.^{11,14} However, despite the significant IOP-lowering effect of trabeculectomy, authors have highlighted the increased risk of complications such as postoperative anterior chamber shallowing and even malignant glaucoma.^{2,5,6,7,8,11,14} They also recommended phaco+IOL as a viable alternative for initial surgical treatment instead of trabeculectomy in PACG management. A meta-analysis comparing phacotrabeculectomy and phaco+IOL surgeries in PACG patients also yielded similar

results.¹⁵ Additionally, the risk of trabeculectomy failure is higher in PACG compared to POAG.^{7,11,15}

The position and thickness of the lens, volume of the anterior chamber, and iris position play a significant role in the pathogenesis of PACG.^{1,2,4,7,8,11,15} Therefore, phaco+IOL surgery is highly effective in achieving glaucoma control, especially in cases where coexisting cataracts are present.1,2,6,12,16 Phaco+IOL also leads to a clinically significant reduction in IOP in PACG cases when compared to normal eyes and cases of POAG.¹⁶ When considering PACG cases for lens extraction, a detailed evaluation of the angle, determination of whether the angle closure is appositional, and assessment of the presence of peripheral anterior synechiae are crucial for the success of the surgery.⁶ Appositional angle closure occurs when factors such as pupillary block or a thick peripheral iris roll are present. Lens extraction allows the iris to assume a more posterior position within the eye, leading to widening of the anterior chamber angle and resolution of appositional angle closure.¹² However, the decision and timing of lens surgery when cataract is not significant remain controversial.^{2,7} In the EAGLE study,² CLE was performed on 208 patients with PAC and PACG at the time of initial diagnosis, while 211 patients received LPI and medical treatment. After a 3-year follow-up, the group that underwent CLE showed better IOP control, improvement in visual quality and daily activity skills, and reduced need for additional glaucoma surgery. The long-term results of the EAGLE study also support the initial findings.9 This study demonstrated the potential benefit of performing early lens surgery in eyes where the lens is a significant component of angle closure, without waiting for the development of cataract.^{2,9} However, these patients were over 50 years old, with lost accommodative ability and without significant advanced glaucoma. It should be noted that young individuals may experience accommodative loss following CLE.¹² Furthermore, it should be considered that due to the structural characteristics of PACG eyes, they may be more prone to complications during and after phaco+IOL surgery.^{2,6,11,12}

Cases where phaco+IOL surgery is more successful in angle closure are those with shallow anterior chambers, where peripheral anterior synechiae have not yet developed, and with more stable preoperative IOP in appositional angle closure.^{8,17} In cases of peripheral anterior synechial closure, phaco+IOL surgery alone does not definitively resolve the issues with the anterior chamber angle.^{6,8,12,18} Combining phaco+IOL with goniosynechialysis show promising results in this situation.^{6,8,17,18} Recent studies conversely found that both interventions significantly reduced IOP, but there was no significant difference between phaco+IOL with and without goniosynechialysis.^{19,20} Additionally, both groups exhibited similarly low rates of complications. Since a significant portion of our participants had appositional PACG, goniosynechialysis was not performed in any case in order to standardize the surgical procedure of study.

Tarongoy et al.⁷ analyzed 22 studies investigating the impact of phaco+IOL surgery on suspected angle closure, angle closure, and PACG. These studies primarily focused on eyes with cataracts that were affecting vision. The analysis showed that more than 65% of patients who underwent phaco+IOL surgery returned to normal IOP without the need for glaucoma medication. Another report by Chen et al.5 evaluated 12 studies involving a total of 495 PACG patients. The mean preoperative IOP value was 20.2 mmHg, and patients were using an average of 1.9 medications. After phaco+IOL surgery, during an average follow-up period of 15.7 months, the mean IOP decreased to 14.2 mmHg and average number of medications used fell to 0.8. This corresponds to a 30% reduction in IOP and a 58% reduction in medication use.5 A meta-analysis conducted by Masis et al.21 also discovered that in patients with PACG, CLE led to a mean IOP reduction of 6.4 mmHg (range: -9.4 to -3.4). Shams and Foster²² reported an average IOP reduction of 3 mmHg in PACG patients after phaco+IOL surgery and emphasized the significant impact of lens surgery for advanced-stage glaucoma patients. However, the authors have also pointed out the high rate of complications in this patient group. Liu et al.¹⁴ noted a decrease in the need for glaucoma medications initially, but an increase over the subsequent 4 years. The long-term results of the EAGLE study also indicated that patients with PACG who undergo CLE have a 10-fold higher rate of achieving IOP control without using antiglaucoma eye drops compared to the group that underwent LPI.9 In the present study, the PACG group had a mean preoperative IOP of 20.1 mmHg and used an average of 2.9 medications, which decreased to 15.1 mmHg and 1.7 medications after surgery. The decrease in IOP was significantly greater in the PACG group compared to the control group.

In various studies, the degree of IOP reduction after phaco+IOL surgery for PACG has been associated with several factors, such as the difference in ACD measurements before and after surgery, as well as a reduction in LT.^{4,14,22,23,24,25,26} Helmy²³

also indicated that ACD and LT are related to postoperative IOP and the number of medications used by PACG patients. In the present study, we observed that postoperative IOP reduction was correlated with preoperative AD and ACD but not preoperative LT. There is only one report in the literature that argues that changes in ACD or LT after surgery are not associated with IOP reduction.²⁷ Additionally, while a reduction in LT was certainly expected after cataract surgery, we believed that quantitatively reporting these data would be valuable in enhancing the comprehensibility of the study.

Although the LT of the PACG group was greater than that of the control group, the preoperative BCVA was lower in the control group. Nevertheless, the significant difference in BCVA between the two groups suggests that cataracts may be at a more advanced stage in the control group. Unfortunately, our inability to quantitatively measure lens densities prevents us from providing objective data to assess nuclear lens opacities. Additionally, the structurally thick lens in PACG patients may indicate the importance of LT in the pathogenesis of the disease.

In cases of mild to moderate glaucoma, multifocal lenses are occasionally used. However, their use is contraindicated in cases with advanced glaucomatous damage because of reported reductions in contrast sensitivity and potential impact on visual field.⁸ Evidence suggests that the best IOL option is aspheric monofocal IOLs, which have been shown to provide a 4-dB improvement in perifoveal threshold values compared to the standard IOL for glaucoma patients.^{8,28} Therefore, singlepiece, aspheric, hydrophobic acrylic, monofocal, foldable IOL (Alcon SA60AT, Alcon Laboratories, Inc.) was implanted in all participants in our study to standardize the surgery.

In the present study, the PACG group exhibited an increase in BCVA, a significant decrease in IOP, an increase in ACD, a decrease in LT, and a significant reduction in the number of antiglaucoma medications used after phaco+IOL surgery. Furthermore, when comparing the preoperative and postoperative differences in these parameters between the PACG and control groups, statistically significant differences were observed. To the best of our knowledge, there is no similar study comparing preoperative and postoperative anterior chamber parameters using the Lenstar in patients with PACG and a control group among Caucasian people. However, the presence of certain limitations should not be overlooked when interpreting the results of the study.

Study Limitations

One limitation of the study was the relatively small sample size and short follow-up duration. A larger sample size and longer follow-up period involving a more diverse participant group would provide more generalizable information about the effects of phaco+IOL surgery in patients with PACG. Another limiting factor that affected the results of our study is the absence of quantitative measurements of iridocorneal angle. Although the presence of generalized peripheral anterior synechiae was ruled out by a skilled clinician through gonioscopic examination, evaluating the iridocorneal angle with objective measurements and comparing it with other parameters would yield more reliable results. As ACD is low in PACG, the probability of endothelial damage during phaco surgery is higher than in open-angle eyes. Therefore, it would be appropriate to compare the preoperative and postoperative endothelial cell counts of the patients in the study design.

Conclusion

In PACG patients, phaco+IOL surgery leads to significant widening of the widening of anterior chamber compared to the control group and allows better control of IOP with fewer antiglaucomatous medications after surgery. Further long-term studies conducted with larger patient series will provide more guidance in this regard.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ankara Training and Research Hospital Ethics Committee (number: 15.09.2021, E-21/661).

Informed Consent: Obtained.

Authorship Contributions

Surgical and Medical Practices: E.Ş., S.B., Concept: E.Ş., S.B., Design: S.B., B.D.Y.E., F.B.A., Data Collection or Processing: M.T., F.B.A., S.B., Analysis or Interpretation: E.Ş., Literature Search: S.B., B.D.Y.E., F.B.A., Writing: S.B.

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