Double stimulation in the same menstrual cycle (DuoStim): a comparative evaluation of follicular and luteal phase response

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Abstract

Objective: Double ovarian stimulation (DuoStim) protocols, in which both follicular and luteal phase stimulations are performed within the same menstrual cycle, have emerged as a promising strategy for patients with diminished ovarian reserve. The aim of this study is to compare the outcomes of follicular and luteal phase stimulations in patients undergoing DuoStim protocols.

Material and Methods: This retrospective intra-patient paired comparative study included patients who underwent DuoStim between January 2018 and December 2024 at a university-based infertility clinic. Stimulation protocols, gonadotropin doses and trigger types were evaluated. Primary outcomes were retrieved oocyte and metaphase II (MII) oocyte numbers across both stimulation phases. Clinical pregnancy rates achieved by embryos derived separately from each stimulation phase were evaluated as a secondary outcome. Duration of stimulation, total gonadotropin doses administered, cumulative oocyte yield and embryos obtained, fertilization rates, implantation rates, and live birth rates were also assessed.

Results: The study included 120 patients. Retrieved oocytes numbers [2 (1-3) and 2 (1-5) in follicular phase and luteal phase], MII oocytes [1 (1-2) and 2 (0-4)], and frozen cleavage stage embryos [1 (0-1) and 1 (0-2) in follicular phase and luteal phase] were higher in the luteal phase stimulation ($p<0.001$, $p=0.001$, and $p=0.005$ respectively). Oocyte yield, fertilization rates, implantation rates, and clinical pregnancy rates were similar between the two phases. Total gonadotropin doses and stimulation duration were significantly higher during follicular phase stimulation.

Conclusion: In patients with diminished ovarian reserve undergoing DuoStim, luteal phase stimulation yielded significantly more retrieved oocytes and MII oocytes despite requiring lower gonadotropin doses and shorter stimulation duration. Fertilization rates, embryo development, and clinical pregnancy rates were comparable between phases, suggesting that luteal phase-derived embryos are equally competent. These findings support DuoStim as an effective strategy to maximize oocyte yield within a single menstrual cycle in this challenging population. Further prospective studies are warranted to evaluate cumulative reproductive outcomes. [J Turk Ger Gynecol Assoc. 2026; 27(3): 196-202]

Keywords: Diminished ovarian reserve, double stimulation, DuoStim, ovarian stimulation

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Introduction

Follicular growth is believed to occur in multiple waves enabling recruitable antral follicles in the ovaries throughout the entire menstrual cycle (1). Based on this physiological understanding, in assisted reproductive technology, particularly in patients with diminished ovarian reserve, two consecutive stimulations may be performed within the same cycle to increase the number of oocytes retrieved in a shorter time and enhance the likelihood of obtaining more embryos (2). However, studies investigating

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this protocol, referred to as "double stimulation" or "DuoStim," remain limited.

It has been reported that better reproductive outcomes can be achieved with the continuation of the second stimulation after the conventional protocol in cases of diminished ovarian reserve (3). Nonetheless, results of studies comparing follicular and luteal phase efficiency are conflicting. Some studies indicate that oocytes retrieved during follicular phase stimulation exhibit higher quality and fertilization rates compared to those from luteal phase stimulation (4,5), while others report a superior ovarian response in luteal phase stimulation or find no significant difference between the two phases (6-8). Moreover, the interval between oocyte retrieval and the initiation of luteal phase stimulation varies across studies, and the optimal timing to achieve the most effective ovarian response is unclear (5).

The aim of this study was to compare the reproductive outcomes of follicular and luteal phase stimulation in patients undergoing double stimulation within the same cycle. A particular question of interest was the comparison of clinical pregnancy rates obtained with embryos derived from both stimulation phases separately.

Material and Methods

This study was conducted as a retrospective intra-patient paired comparative study. Data of patients who underwent two consecutive stimulations double ovarian stimulation (DuoStim) in the same cycle between January 2018 and December 2024 in the Reproductive Endocrinology and Infertility Department of a Başkent University Faculty of Medicine were evaluated. Follicular phase- and luteal phase-derived oocytes and embryos, along with pregnancy outcomes obtained from these embryos, were compared. All patients who completed both stages of sequential stimulation in the same cycle due to diminished ovarian reserve/poor ovarian response during this period were included in the study. Diminished ovarian reserve is defined as anti-Müllerian hormone (AMH) <1.1 ng/mL or antral follicle count <7 (9). Patients with known endometrial anomalies, genetic anomalies, and recurrent implantation failure were excluded. Pre-implantation genetic testing cycles were not included.

Stimulation protocols

In our clinic, antagonist or progestin-primed ovarian stimulation (PPOS) protocols are routinely employed for controlled ovarian stimulation. Ovulation induction regimens were tailored to each patient's age, body mass index (BMI), and antral follicle count during both stimulation phases at the clinician's discretion. In the antagonist protocol, cetrorelix acetate (Cetrotide®, Merck, France) was initiated on the sixth day following the administration of 150-300 IU/day of gonadotropins, including follicle-stimulating hormone [(FSH); Gonal-f®, Merck, Italy] and/or human menopausal gonadotropin (Meriofert®, IBSA, Switzerland) (10). In the PPOS protocol, dydrogesterone (Duphaston® 10 mg, Abbott, Türkiye) was administered at a dose of 20 mg/day (2×10 mg) alongside gonadotropins (11). When at least one to two follicles reached ≥18 mm in diameter, final oocyte maturation was triggered using human chorionic gonadotropin [(hCG); Ovitrelle® 250 mcg, Merck, Türkiye] and/or a GnRH agonist (Decapeptyl® 0.1 mg, Ferring, Germany), and oocyte retrieval was performed 36 hours after the trigger (10).

Patients with diminished ovarian reserve were evaluated by ultrasonography at the oocyte retrieval day and if two or more follicles ≤10 mm were observed in one or both ovaries, luteal phase stimulation was initiated on the same day or within 6 days after oocyte retrieval. The preferred stimulation protocols and trigger agents were decided by clinical judgement. When at least one follicle reached ≥18 mm during the luteal phase, final triggering and oocyte retrieval were scheduled 36 hours later.

Retrieved oocytes were assessed for maturity, and intracytoplasmic sperm injection was performed on metaphase II (MII) oocytes. Fertilization was confirmed by the presence of two-pronuclear (2PN) zygotes 16-18 hours post-injection. Cleavage stage embryos were frozen on day 3, and blastocysts were cryopreserved on day 5/6. Only good-quality cleavage stage embryos and blastocysts were frozen. Good quality embryos were defined as cleavage stage embryos with ≥7 blastomeres, ≤10% fragmentation, uniform blastomeres, no or minimal vacuoles, and normal zona pellucida (Grade A or B); blastocysts were considered good quality at 3BB and above according to Gardner's classification (12).

Frozen embryo transfer protocol

All embryo transfers were frozen-thawed transfers performed with artificially prepared endometrium using hormone replacement therapy. Estradiol (E_2) hemihydrate (Estrofem® 2 mg, Novo Nordisk A/S, Denmark) 6 mg/day was initiated at day 3 of menstrual cycle and continued for at least 12 days. Endometrial thickness was measured by interval ultrasonography, and vaginal progesterone (P) (Progestan® 200 mg, Koçak Farma, Türkiye) 800 mg/day and subcutaneous P (Prolutex® 25 mg, IBSA, Türkiye) 25 mg/day were administered provided that endometrial thickness was ≥7 mm (11,13). Embryo transfer was performed on the fourth day of P supplementation for cleavage-stage embryos and on the sixth day for blastocyst-stage embryos (13). The presence of pregnancy was evaluated by measuring serum b-hCG value 12 days after embryo transfer. Clinical pregnancy was defined as presence of fetal cardiac activity on ultrasound investigation.

Outcome measures

Patient characteristics, including age, BMI and AMH levels were recorded. Cycle-related parameters, such as the stimulation protocols used in the follicular and luteal phases, duration of stimulation, total gonadotropin doses, trigger agents, and hormone levels on the trigger day were evaluated.

Primary outcomes were the cumulative number of oocytes retrieved and MII oocytes across both stimulation phases, reflecting the principal aim of DuoStim in this population. As a secondary outcome, clinical pregnancy rates achieved by embryos derived separately from each stimulation phase were compared. Additional secondary outcomes included fertilization rates, implantation rates, duration of stimulation, and total gonadotropin doses administered. The effect of the interval between oocyte retrieval and the initiation of luteal phase stimulation was also assessed.

Oocyte yield was defined as the ratio of the number of oocytes retrieved to the number of follicles ≥10 mm on the day of oocyte retrieval. Fertilization rate was defined as the ratio of 2PN zygotes to the number of MII oocytes used for fertilization. Implantation rate was calculated as the number of gestational sacs per embryo transferred. Pregnancy rate was defined as the number of clinical pregnancies per oocyte retrieval cycle from which an embryo transfer was performed (10).

This study was performed in line with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of the Başkent University where the study was conducted (approval no: KA25/193; date: 19/06/2025). Informed consent for the use of medical data was obtained from all patients prior to their treatment.

Statistical analysis

SPSS, version 27.0 was used in the analysis of the data (IBM Inc., Armonk, NY, USA). Categorical measurements are presented as numbers and percentages, and continuous measurements are summarized with mean and standard deviation. For within-patient paired comparisons of continuous variables, paired sample t-tests were used when data were normally distributed, and Wilcoxon signed-rank tests were applied otherwise. For comparison of within-patient categorical variables McNemar's test was used. The effect of timing of luteal phase stimulation initiation on luteal phase outcomes were evaluated by Mann-Whitney U test (continuous variables) and chi-square test (categorical variables). In all tests, $p<0.05$ was considered statistically significant.

Results

A total of 120 patients who completed both phases of the double stimulation protocol during the specified study period were included. The mean age was 35.82±5.09 years, mean BMI was 24.04±4.04 kg/m^2, mean AMH level was 0.68±0.43 ng/mL, and mean antral follicle count was 5.21±2.63 (Table 1). The duration of stimulation and the total gonadotropin doses administered were significantly greater during follicular phase stimulation ($p<0.001$). The antagonist protocol was more frequently used during follicular phase stimulation (55.1%), whereas the PPOS protocol was predominantly used in luteal phase stimulation (81.3%) ($p<0.001$). On the trigger day, E_2 and P levels were significantly higher in luteal phase stimulation. Although dual trigger was widely used in both stimulation phases, it was significantly more frequent in the luteal phase (73.9%) ($p<0.001$) (Table 2). In follicular phase stimulation, there were no significant differences in retrieved oocyte rates, fertilization rates, frozen embryo rates, or implantation rates across different trigger types ($p>0.05$). However, in luteal phase stimulation, the fertilization rate was significantly higher in the dual trigger group ($p<0.001$).

Compared to follicular phase stimulation, luteal phase stimulation yielded a significantly higher number of retrieved oocytes [2 (1-3) vs. 2 (1-5) in follicular and luteal phases, respectively; $p<0.001$] and MII oocytes [1 (1-2) vs. 2 (0-4) in follicular and luteal phases, respectively; $p=0.001$]. Frozen cleavage embryo rates were also higher in luteal phase simulation [1 (0-1) vs. 1 (0-2); $p=0.005$] while frozen blastocyst numbers were similar between the two phases (Table 2).

Embryos were thawed for transfer in 68 of the 120 patients (56.7%): 43 patients had follicular phase embryos thawed and 43 had luteal phase embryos thawed, with 18 patients having embryos from both phases thawed. Embryo transfer was performed in 66 patients; transfer of follicular phase embryos in 5 patients, and luteal phase embryos in 4 patients, were deferred due to poor embryo quality following the thawing process.

Table 1. Baseline clinical characteristics of included patients

Clinical characteristics	Mean ± SD
Age (years)	35.82±5.09
BMI (kg/m^2)	24.04±4.04
AMH (ng/mL)	0.68±0.43
AFC	5.21±2.63

Values are presented as mean ± SD. AMH: Anti-Müllerian hormone, AFC: Antral follicle count, BMI: Body mass index, SD: Standard deviation

Table 2. Comparison of cycle parameters and outcomes between follicular and luteal phase stimulations (n=120 for each phase unless otherwise noted)

		Follicular phase stimulation (n=120) Median (IQR)	Luteal phase stimulation (n=120) Median (IQR)	p
Stimulation duration (days)		7 (6-9)	6 (4-8)	**0.004**
Total gonadotropin dose (IU)		2100 (1500-2700)	1500 (1068.7-2306.2)	**0.002**
Stimulation protocol, n (%)				**<0.001**
	None	4.2	3.6	
	Antagonist	56.8	15.2	
	PPOS	39.0	81.3	
E_2 at trigger day (pg/mL)		333 (206.5-559)	495 (265-887.7)	**<0.001**
P at trigger day (ng/mL)		0.3 (0.2-0.4)	6.6 (1.4-12.9)	**<0.001**
Trigger type, n (%)				**<0.001**
	hCG	35.6	24.3	
	Agonist	22.9	1.7	
	Dual	41.5	73.9	
Follicles ≥10 mm at trigger day		2 (1-3)	4 (2-6)	**<0.001**
Oocytes retrieved, n		2 (1-3)	2 (1-5)	**<0.001**
MII oocytes, n		1 (1-2)	2 (0-4)	**0.001**
Oocyte yield (%)[1]		100 (50-100)	73.2 (33.3-100)	0.191
Fertilization rate (%)[2]		50 (0-100) (n=104)	50 (33.3-89.3) (n=98)	0.160
Group-level proportion (%)[3]		67.9% (127/187)	65.3% (186/285)	
Cleavage-stage embryos, n[4]		1 (1-2) (n=72)	2 (1-3) (n=78)	**0.007**
Blastocysts, n[4]		0 (0-0)	0 (0-0)	0.348
Frozen cleavage embryos, n[4]		1 (0-1)	1 (0-2)	**0.005**
Frozen blastocysts, n[4]		0 (0-0)	0 (0-0)	0.348

[1]Oocyte yield = oocytes retrieved/follicles ≥10 mm on trigger day. Calculated only for patients with ≥1 follicle ≥10 mm. [2]Fertilization rate = 2PN zygotes/MII oocytes used for ICSI. Denominator reduced to n=104 (follicular) and n=98 (luteal) because patients with 0 MII oocytes were excluded from the fertilization rate calculation. [3]Fertilization rate: group-level proportions (total 2PN/total MII oocytes). [4]Cleavage embryo number reported only for patients with ≥1 fertilized oocyte (n=72 follicular, n=78 luteal). E_2: Estradiol, P: Progesterone, hCG: Human chorionic gonadotropin, MII: Metaphase II, PPOS: Progestin-primed ovarian stimulation, IQR: Interquartile range, 2PN: Two-pronuclear. Values are mean ± standard deviation or n (%)

Table 3. Transfer outcomes of embryos derived separately from follicular and luteal phase stimulations

	Follicular phase	Luteal phase	Both phases	p
Patients with embryos thawed, n (%) (n=68)	43 (35.8%)	43 (35.8%)	18	
Patients with embryos transferred, n (%) (n=66)	38 (31.7%)	39 (32.5%)	11	
Transferred embryos, n median (IQR)	1 (1-1) (n=38)[1]	1 (1-2) (n=39)[2]		0.157
Implantation rate (%)[3] median (IQR)	0 (0-100) (n=38)	0 (0-50) (n=39)		0.705
Clinical pregnancy rate, % (n)	50.00 (n=19/38)	41.02 (n=16/39)		0.564
Live birth rate, % (n)	23.68 (n=9/38)	33.33 (n=13/39)		0.157

[1]Follicular phase transfers: 30 patients received 1 embryo, 8 received 2 embryos; 5 patients had embryos thawed but not transferred due to poor post-thaw quality. [2]Luteal phase transfers: 22 patients received 1 embryo, 16 received 2 embryos, 1 received 4 embryos; 4 patients had embryos thawed but not transferred due to poor post-thaw quality. [3]Implantation rate = gestational sacs / embryos transferred. Note: 18 patients had embryos from both phases thawed; 11 had transfers from both phases. Transfer outcomes are reported per phase, not per patient. Clinical pregnancy defined as presence of fetal cardiac activity on ultrasound. IQR: Interquartile range

Implantation, clinical pregnancy and live birth rates of embryos derived from the follicular and luteal phases were not statistically significantly different (Table 3).

Initiation day of luteal phase stimulation (oocyte retrieval day/next day vs. ≥2 days after oocyte retrieval) was not found to be associated with clinical pregnancy outcomes (Supplementary Table 1).

Discussion

In this study, which included 120 patients undergoing the DuoStim protocol, luteal phase stimulation yielded a significantly higher number of retrieved oocytes, MII oocytes and frozen cleavage stage embryos compared to follicular phase stimulation. Despite this difference in achieved oocytes, fertilization rates, implantation rates, and clinical pregnancy rates of embryos derived separately from each stimulation phase were comparable between the two phases.

The DuoStim protocol, involving two consecutive ovarian stimulations during the follicular and luteal phases of the same menstrual cycle, was first described by Kuang et al. (6) and is also referred to as the Shanghai protocol. This approach aims to increase the yield of usable oocytes and is particularly useful in cases where a single stimulation is inadequate or when time constraints preclude multiple cycles. As DuoStim minimizes the interval between successive oocyte retrievals, it is especially favored for fertility preservation in patients with medical or social indications (14). In addition, it has been proposed as a viable option for patients with poor ovarian response (7,15).

In our study, both the duration of stimulation and the total gonadotropin dose were higher during follicular phase stimulation. However, contrary findings have been reported, with some studies suggesting that luteal phase stimulation requires a longer duration and higher gonadotropin consumption (5,10). The shorter stimulation duration observed in the luteal phase in our cohort may be attributed to elevated E_2 and P levels. It has been proposed that supraphysiological E_2 and P levels during the luteal phase enhance follicular synchronization and increase the expression of FSH receptors on granulosa cells (16,17). Furthermore, animal studies have demonstrated that high hormonal levels may improve FSH sensitivity of granulosa cells through increased angiogenic factor expression (18). These mechanisms may also contribute to the higher number of oocytes and MII oocytes obtained in the luteal phase in our study.

Our study also revealed comparable fertilization and implantation rates, used as indicators of embryo quality, between follicular and luteal phase stimulations. The BISTIM study which compared DuoStim with two conventional ovarian stimulations in a randomized controlled design, found no difference in reproductive outcomes between the two protocols (19). However, there are few studies comparing the efficiency of follicular and luteal stimulations within the same menstrual cycle, and they have reported conflicting results. While some studies have indicated a diminished response during luteal phase stimulation (4,5), higher oocyte yield during the luteal phase has also been demonstrated (20). In a study by Zhang et al. (21), although stimulation duration and total gonadotropin dose were similar between the two phases, a greater number of oocytes were retrieved during luteal phase stimulation. However, the rate of MII oocytes was lower in the luteal phase, and both cleavage-stage and high-quality embryo rates were comparable between the two phases (21). Cimadomo et al. (16) reported fewer oocyte and blastocyst numbers in follicular phase stimulation. However, pregnancy and delivery rates were similar between follicular phase and luteal phase derived blastocytes (16). In the study of Luo et al. (10), fertilization and frozen embryo rates were similar in both groups, although implantation and pregnancy rates per transfer appeared to be more favorable with embryos derived from luteal phase stimulation. Despite these discrepancies, it has been stated that patients with poor ovarian response who fail to achieve good quality embryos after the first stimulation are more likely to continue stimulation in the same cycle, rather than waiting for a subsequent cycle. As a result, the likelihood of transferring at least one euploid embryo may be higher following a DuoStim protocol compared to two separate conventional stimulations (15). Indeed, previous reports have suggested that DuoStim can increase the number of retrieved oocytes and improve the chance of embryo transfer (2,22,23). Importantly, unlike most published studies that report only oocyte and embryo yield, the present study separately attributes clinical pregnancy outcomes to each stimulation phase, which represents a relatively uncommon approach in the DuoStim literature.

Various stimulation protocols have been described in the literature for both follicular and luteal phases (5,24). In our study, the antagonist protocol was predominantly used during follicular phase stimulation, while the PPOS protocol was more frequently applied in the luteal phase. A previous study employing similar protocols reported no significant differences in embryo quality between the two stimulation phases (10). Also, a recent investigation examining the effects of different follicular phase protocols on subsequent luteal phase outcomes in DuoStim cycles found that both antagonist and PPOS protocols were associated with favorable results with no significant differences (25). Since frozen embryo transfer policies are mandatory in double stimulation cycles, PPOS protocol may present additional advantages in the luteal phase, including lower cost, fewer injections, and prevention of premature menstruation before the second oocyte retrieval.

The choice of trigger was left to the clinician's discretion. Therefore, various trigger protocols including hCG trigger, gonadotropin-releasing hormone (GnRH) agonist trigger and dual

trigger, which combines GnRH agonist with hCG, were utilized in the present study. Dual trigger has been reported to improve the number of oocytes retrieved and enhance reproductive outcomes in patients with poor ovarian response undergoing *in vitro* fertilization (IVF) (17,26), and is often preferred due to these advantages. In the present study, trigger agents were not uniform. Dual trigger was used in 73.9% of luteal phase stimulations and was associated with significantly higher fertilization rates in the luteal phase. The more frequent use of dual trigger at the end of cycles characterized by supraphysiological hormone levels may have further contributed to this finding.

Current literature lacks consensus regarding the optimal interval between oocyte retrieval and initiation of luteal phase stimulation. This interval has been reported to vary from 1 day to 7 days post-retrieval in different studies (3,5,10,24). In a recent large retrospective study, 541 DuoStim cycles were grouped based on the timing of luteal phase stimulation initiation, from 0-2 to 5-6 days, and no significant difference in oocyte yield was found among the groups (27). Consistent with this, no significant differences were observed in our study when luteal phase stimulation was initiated at oocyte retrieval day/next day versus ≥2 days after retrieval (Supplementary Table 1), suggesting flexibility in the application of IVF procedures without strict timing constraints.

Study limitations

The principal strength of this study lies in its reporting of clinical pregnancy rates separately attributable to embryos derived from each stimulation phase within the DuoStim cycle. This approach, which is uncommon in the existing literature, enables a direct comparison of embryo competence between the follicular and luteal phases. The intra-patient design eliminates between-patient confounding, and the cohort of 120 patients represents one of the larger series of this kind reported to date.

However, several limitations of this study merit consideration. First, the retrospective design precludes causal inference, and the non-predefined decision to proceed with luteal phase stimulation introduces substantial selection bias. The decision to initiate luteal phase stimulation was made at oocyte retrieval based on the presence of residual follicular activity on ultrasound, meaning that only patients with at least some remaining follicular potential were included in the DuoStim cohort. This selective inclusion may have favored patients with relatively better ovarian reserve within the poor responder spectrum and may have contributed to the higher oocyte yield observed in the luteal phase.

Second, a formal a priori power calculation was not performed, given the retrospective nature of the study and the limited published data on phase-specific clinical pregnancy rates in DuoStim cycles. This should be considered when interpreting the absence of statistically significant differences in pregnancy outcomes.

Third, stimulation protocols and trigger types differed substantially between follicular and luteal phase stimulations, reflecting routine clinical practice rather than a standardized experimental design. Multivariable adjustment for these protocol differences was not feasible given the sample size. However, given the lack of standardized protocols in the currently limited literature, such variability is not unusual. Finally, embryo transfer was not performed in all patients with frozen embryos, and clinical pregnancy and live birth data were available for only a limited number of patients at the time of analysis.

Conclusion

Our findings indicate that in patients with diminished ovarian reserve undergoing DuoStim, luteal phase stimulation yielded significantly more retrieved oocytes, MII oocytes, and frozen cleavage-stage embryos despite requiring lower gonadotropin doses and shorter stimulation duration. Nevertheless, fertilization rates, implantation rates, and clinical pregnancy rates were comparable between the two phases, suggesting that luteal phase-derived embryos are equally competent to those from the follicular phase. While double stimulation cycles require frozen embryo transfer, luteal phase stimulation appears to be at least as effective as follicular phase stimulation within the same cycle and may contribute to an increased number of transferable embryos in patients with diminished ovarian reserve. Therefore, evaluation of these patients at the end of the follicular phase, with subsequent referral of suitable candidates to a DuoStim protocol, may improve their reproductive outcomes. Further randomized prospective studies are warranted to refine stimulation protocols and evaluate cumulative reproductive outcomes in women with diminished ovarian reserve.

Ethics

Ethics Committee Approval: *This study was performed in line with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of the Başkent University where the study was conducted (approval no: KA25/193; date: 19/06/2025).*

Informed Consent: *Informed consent for the use of medical data was obtained from all patients prior to their treatment.*

Footnotes

Author Contributions: *Surgical and Medical Practices: G.D.D., D.A.Y., S.Y., P.Ç.A., E.Ş., Concept: E.Ş., Design: G.D.D., E.Ş., Data Collection or Processing: G.D.D., D.A.Y., S.Y., Analysis or Interpretation: G.D.D., E.Ş., Literature Search: G.D.D., E.Ş., Writing: G.D.D., E.Ş.*

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Supplementary Table 1: *https://d2v96fxpocvxx.cloudfront.net/d87fe3be-5485-41db-ae31-897b8342c583/content-images/29411dad-41ab-4a0c-82db-0f504325cd81.pdf*

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