

Risk of Hypocalcemia and Osteoporosis due to Vitamin D Deficiency in Patients Undergoing Sleeve Gastrectomy and Bypass Surgery for Obesity

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ABSTRACT

Introduction: Obesity is a chronic disease that is increasing worldwide. It is known that mineral and vitamin deficiencies develop in obese individuals. Surgical treatment options are becoming increasingly common for the permanent and effective treatment of obesity. It was observed that mineral and vitamin deficiencies increased after surgical interventions. The aim of this study was to investigate the efficacy of laparoscopic sleeve gastrectomy (LSG) and combined Roux-en-Y Gastric Bypass (RYGB) methods for weight loss in obese patients and their effects on vitamin D, calcium⁺² (Ca⁺²), parathyroid hormone (PTH), and P levels and the risk of osteoporosis in patients after surgery.

Methods: The study included 50 patients who underwent LSG and 47 patients who underwent RYGB. Routine preparations and standard surgical procedures were performed. Body mass index, blood vitamin D, Ca⁺², PTH, and P levels were measured preoperatively and postoperatively at 3-month intervals for 12 months. Data were analyzed using independent and dependent t-tests.

Results: Preoperative hypocalcemia was observed in both groups (LSG: 14%, RYGB: 19.1%). It was observed that both surgical methods were effective for weight loss. Postoperative hypocalcemia rates increased in both groups (LSG: 26%, RYGB: 33.3%). After vitamin and mineral supplementation, hypocalcemia rates improved but could not be brought to normal levels. In addition, decreased vitamin D and PTH levels were observed after the surgical intervention.

Conclusion: Low vitamin D and Ca⁺² levels were increased in patients after bariatric surgery. Mineral and vitamin supplementation decreased these decreases but did not increase their normal levels. This treatment is thought to increase the risk of osteoporosis. It would be useful to investigate the effects of higher-dose supplements.

Keywords: Obesity, bariatric surgery, vitamin D, Ca⁺², hypocalcemia, PTH and P, osteoporosis

Introduction

Obesity is a chronic disease that is increasing worldwide (1). The first treatment methods to be tried are lifestyle changes, diet, exercise, medication, and hormonal therapies. However, surgical treatment may be required when these methods are inadequate (2). Laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y Gastric Bypass (RYGB) are the two most commonly used methods for the treatment of obesity (3). In these surgical methods, changes are made in the anatomy of the gastrointestinal

system, which may affect vitamin and mineral absorption. Vitamin and mineral deficiencies, such as vitamin D, calcium⁺² (Ca⁺²), and potassium, are known to be present in obese patients. It can be predicted that deficiencies in these values may increase after surgical treatment. However, there is limited information on vitamin D, Ca⁺², parathyroid hormone (PTH), and P levels in patients undergoing bariatric surgery after surgical interventions. In this study, we aimed to compare the preoperative and postoperative vitamin D, Ca⁺², PTH, and P levels of patients undergoing LSG and RYGB.



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Methods

In our study, we retrospectively evaluated the data of 97 patients who underwent bariatric surgery for obesity between 01.01.2015-01.03.2016 at University of Health Sciences Turkey, İstanbul Training and Research Hospital. The study was approved by the Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 164, date: 20.05.2022). Informed consent was obtained from the patients. The first group (group 1) included patients who underwent sleeve gastrectomy surgery, which is a volume restriction method, and the second group (group 2) included patients who underwent RYGB surgery, which is a volume restriction and malabsorption method. Twenty-four male and 73 female patients were included in the study. Birth dates, sex, height, weight, Ca, phosphorus, PTH, and vitamin D levels were recorded preoperatively and at 3, 6, 9, and 12 months. Patients with missing preoperative and postoperative laboratory data were excluded from the study.

Statistical Analysis

Prior to further analyses, Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of the variables. Non-parametric methods were used for non-normally distributed variables. Subsequently, the Mann-Whitney U test was used to compare the variables obtained from the measurements between groups. Chi-square and Fisher's exact tests were used to analyze the relationships or differences between groups regarding categorical variables. Repeated measures tests was used for comparison of repeated measurements. Periodic comparisons of values were performed using the paired sample t-test. Comparative results between groups based on other demographic characteristics are presented as the ratio of qualitative variables. Quantitative variables are expressed as mean and standard deviation. Statistical analysis was performed using the SPSS, version 22.0 (SPSS Inc., Chicago, IL, USA). A p-value of <0.05 was considered statistically significant.

Results

Preoperative demographic characteristics, weight-height measurements, body mass index (BMI), mean age, Ca²⁺, phosphorus

(P), PTH, and vitamin D values of the patients included in the study are presented in Table 1.

Preoperative height, Ca²⁺, PTH, and vitamin D values were similar between the patients were similar ($p>0.05$). The mean weight and BMI of the patients in group 1 were significantly lower in group 1 than in group 2 ($p<0.001$). The age of those in group 2 was higher than that of group 1 ($p=0.006$).

The postoperative body weight changes of the groups are shown in Table 2, Figure 1.

There was a significant difference between the body weights of both groups. Although this difference decreased over time, it remained statistically significant. In all follow-up periods, the weight of patients in group 2 was higher than that of patients in group 1 ($p<0.001$).

It was observed that both groups lost weight significantly in the measurements made in the 3-month periods, and this significance continued to decrease steadily from the date of surgery until the 12th month when the last controls were made ($p<0.001$) (Table 2, Figure 1).

The difference between the BMIs of both groups decreased over ($p<0.001$).

It was observed that both groups lost weight and their BMIs decreased significantly in the measurements performed at 3-month intervals ($p<0.001$) (Table 2, Figure 2).

The measured Ca²⁺ values of the groups are shown in Table 2, Figure 3.

Ca values were similar between the groups in almost every period. Only in the 9th month was the Ca value slightly higher in group 2 ($p=0.037$). In addition, no regular increase or decrease in Ca value was detected during the follow-up. In group 1, preoperative Ca values were significantly higher than those in the 3rd, 6th, and 9th months ($p=0.009$). In group 2, preoperative Ca values were significantly higher than those in the 3rd and 9th months ($p=0.016$).

The P levels of the groups are shown in Table 2, Figure 4. No significant difference in phosphorus values was observed between the groups in phosphorous values ($p>0.05$). In addition, when each group was

Table 1. Demographic and clinical data of the patients

	Sleeve gastrectomy (I)	Roux N-Y gastric bypass (II)	p
Age	47.9±10.3	55.2±14.3	0.006
Gender			
Male	14 (28%)	7 (14.9%)	0.14
Female	36 (72%)	40 (85.1%)	
Height (cm)	164.4±9	161.8±8.4	0.16
Preoperative weight (kg)	137.2±116.3	141.4±16	<0.001
Preoperative BMI (kg/m ²)	44.6±5.5	53.7±6.5	<0.001
Preoperative Ca (mg/dL)	9.3±0.7	9.3±0.5	0.66
Preoperative P (mg/dL)	3.7±0.4	3.9±0.8	0.58
Preoperative PTH (IU)	58.2±25.3	56.6±23.5	0.75
Preoperative vitamin D (IU)	14±6.6	19.5±13.1	0.045

BMI: Body mass index, Ca: Calcium, P: Phosphorus, PTH: Parathyroid hormone

evaluated individually, no regular increase or decrease in phosphorous value was detected during follow-up. In group 1, preoperative phosphorus value was significantly lower than in the 3rd, 6th, 9th, and 12th months ($p < 0.001$). In addition, the phosphorus value in the 3rd month was lower than in the 6th, 9th, and 12th months ($p < 0.001$). In group 2, preoperative phosphorus value was significantly lower than in the 3rd, 6th, 9th, and 12th months ($p < 0.001$).

The PTH values of the groups are presented in Table 2, Figure 5. PTH levels did not differ significantly between the groups ($p > 0.05$). In

addition, when each group was evaluated individually, no regular increase or decrease in PTH levels was detected during follow-up.

Vitamin D values are shown in Table 2, Figure 6. Vitamin D level was found to be higher in group 2 only in the preoperative period ($p = 0.045$). No significant difference was observed between the two groups during the other periods. In addition, when each group was evaluated individually, no regular increase or decrease in vitamin D value was detected during follow-up.

Table 2. Clinical and laboratory data of the groups

		Sleeve gastrectomy (I)	Roux N-Y gastric bypass (II)	p
Weight (kg)	Preoperative	137.2±116.3	141.4±16	<0.001
	3 rd month	105.5±17.2	122.7±15.1	<0.001
	6 th month	93.7±15	107±14.3	<0.001
	9 th month	85±13.4	94.3±12.3	<0.001
	12 th month	78.3±11.7	83.8±10.6	0.005
	p	<0.001	<0.001	
BMI (kg/m ²)	Preoperative	44.6±5.5	53.7±6.5	<0.001
	3 rd month	39±5.3	47±5.9	<0.001
	6 th month	34.6±4.8	41.3±5.5	<0.001
	9 th month	31.5±4.5	36.1±4.6	<0.001
	12 th month	29±4	32.1±4.1	<0.001
	p	<0.001	<0.001	
Calcium (mg/dL)	Preoperative	9.3±0.7 ^{a-c}	9.3±0.5 ^{a,b}	0.66
	3 rd month	9.1±0.8 ^{d-f}	8.9±0.7 ^a	0.24
	6 th month	8.9±0.8 ^{a,d}	9.1±0.8	0.16
	9 th month	8.8±0.7 ^{b,e}	9±0.6 ^b	0.037
	12 th month	8.9±0.7 ^{c,f}	9.1±0.5	0.07
	p	0.009	0.016	
Phosphorus (mg/dL)	Preoperative	3.7±0.4 ^{a-d}	3.9±0.8 ^{a-d}	0.58
	3 rd month	3.8±0.5 ^{a,e-g}	4.2±0.8 ^a	0.17
	6 th month	4.1±0.6 ^{b,e}	4.2±0.6 ^b	0.61
	9 th month	4.2±0.5 ^{c,f}	4.3±0.7 ^c	0.20
	12 th month	4.1±0.5 ^{d,g}	4.3±0.6 ^d	0.13
	p	<0.001	<0.001	
Parathyroid hormone (IU)	Preoperative	58.2±25.3	56.6±23.5	0.75
	3 rd month	60.5±27.1	63.2±31.9	0.65
	6 th month	55±20.8	63.7±27.5	0.08
	9 th month	53.3±19.1	58.9±20	0.16
	12 th month	52.4±17.8	59.4±24.2	0.11
	p	0.06	0.06	
Vitamin D (IU)	Preoperative	14±6.6	19.5±13.1	0.045
	3 rd month	14.5±7.3	19±11.1	0.08
	6 th month	17.5±10.5	21.8±14.7	0.10
	9 th month	18±12.7	20.6±13.5	0.23
	12 th month	19.3±20.7	21±12.8	0.06
	p	0.13	0.55	

^{a-g}: There was a statistically significant difference at the $p < 0.05$ level between the subgroups marked with the same letters. BMI: Body mass index

Discussion

Today, obesity is a major public health problem, and it is widespread worldwide (1). Obesity was first recognized as a chronic disease by the World Health Organization in 1994 (4). In 1992, Colditz (5) identified obesity as a major risk factor for several chronic diseases (6).

Today, there are not many treatment options for obesity, which has become a major health problem and is gradually increasing. In the 90s, when attention was drawn to the health hazard of obesity, it was emphasized that medical and non-surgical treatment methods were not successful in weight loss and that patients who lost weight quickly returned to their old weight (7). In addition, in various consensus meetings, it has been stated that non-surgical treatments applied in morbidly obese patients have a low chance of success, and surgery

is the most successful method to achieve permanent weight loss (8,9). Various surgical methods have long been recommended and applied for the permanent and effective treatment of obesity and its comorbidities (8,10,11).

In various studies, obese people were found to develop serious metabolic problems and various mineral and nutrient deficiencies occur (9,12-16). In addition, surgical methods applied for the treatment of obesity have been reported to cause the development of various vitamin and mineral deficiencies, although they are very successful in weight loss and correcting metabolic problems (15,17). Clinical studies have shown that problems such as anemia and bone demineralization occur after surgical interventions (18). Frame-Peterson et al. (9) a large literature review reported that surgical interventions provided

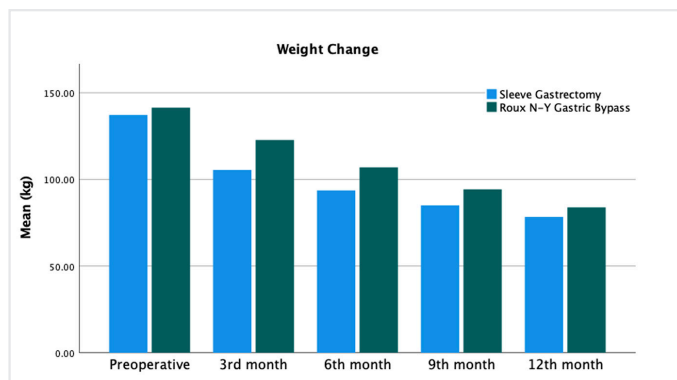


Figure 1. In-group changes in body weight values of both groups

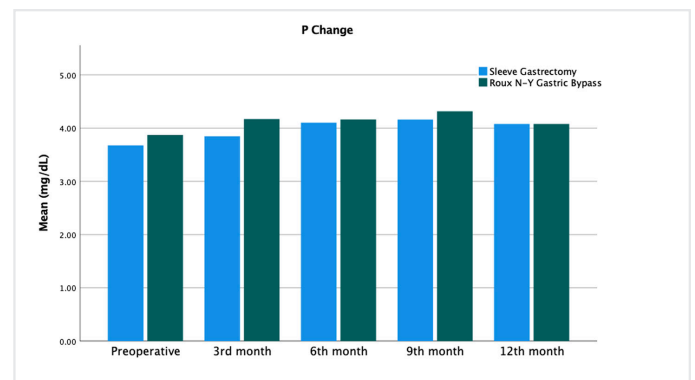


Figure 4. In-group changes in phosphorous values of both groups

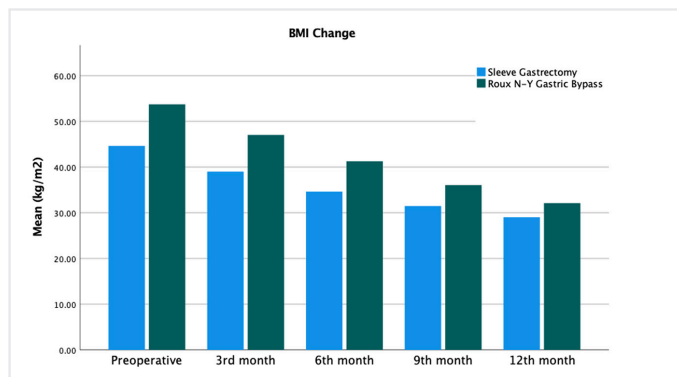


Figure 2. In-group changes in body mass index of both groups
BMI: Body mass index

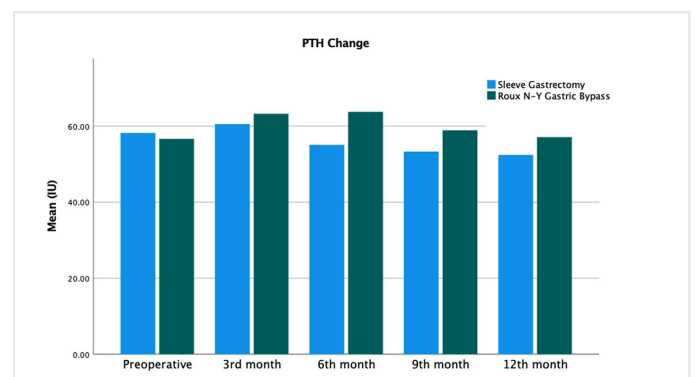


Figure 5. In-group changes in parathyroid hormone values of both groups
PTH: Parathyroid hormone

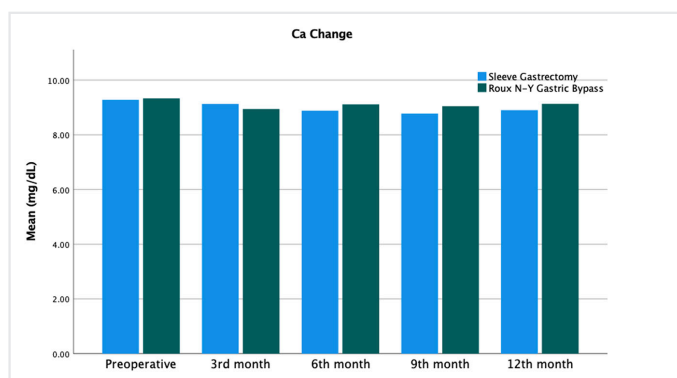


Figure 3. In-group changes in calcium values of both groups

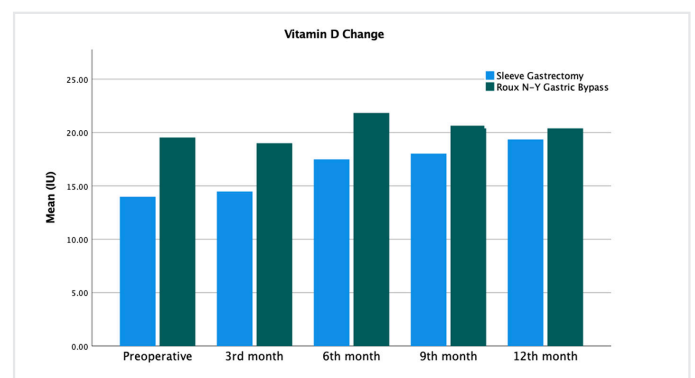


Figure 6. In-group changes in vitamin D values of both groups

effective and permanent weight loss, but severe nutritional deficiencies developed.

In our study, it was determined that 2 different surgical methods (LSG and RYGB) that we applied for the treatment of obesity effectively caused weight loss in patients (Table 2). The weight difference between the groups before and after the operation was gradually reduced. However, the difference continued to decrease at 12 months. The effects of the applied surgical methods on weight loss were in accordance with many clinical studies on this subject (8,10,12).

Ugale et al. (10) in their review emphasizing that obesity is a life-threatening pandemic disease, the authors stated that the success of bariatric surgery increased after the 1980s in parallel with technological developments. In the same study, it was reported that LSG and RYGB provided 50-75% of the excess weight in the body in a similar manner, and both methods were reported to be successful in weight loss. Lager et al. (19) In their study presenting their own clinical series, the authors stated that LSG and RYGB were similarly successful in weight loss.

In our study, we investigated vitamin D deficiency, hypocalcemia and related osteoporosis, which is a common public health problem, in obese people and the pathological conditions that occur after surgical interventions and the measures that can be taken to prevent the occurrence of these pathological conditions.

Costa et al. (12) In their clinical study, they reported that 29% of obese patients had hypocalcemia, and this rate increased to 63% after bariatric surgery. Many clinical studies on this subject have emphasized that vitamin D deficiency, hypocalcemia, and related hyperparathyroidism develop especially after bariatric surgical interventions with malabsorptive properties (9,12,13,18-21).

Costa et al. (12) they explained the reasons for the development of vitamin D insufficiency in obese people as inadequate exposure to sunlight, low mobility, overdressing, inadequate vitamin D intake, inadequate 25-hydroxylation process in the liver as a result of fatty liver developing due to obesity, and dilution of vitamin D by storage in adipose tissue, which is excessive in obese people.

Vitamin D insufficiency or deficiency in obese people causes a decrease in Ca^{+2} absorption from the intestines. The resulting hypocalcemia stimulates the release of PTH. Increased PTH attempts to balance hypocalcemia by causing the release of Ca^{+2} from the bone. However, demineralization, which is expressed as bone resorption, develops during this process, and pathological fractures may occur (12,18).

In this clinical study, patients were divided into 2 groups. A statistical significance was found between the groups in terms of BMI. It is clear that this difference was influenced by the inclusion of overweight patients in the 2nd group, as malabsorptive methods (RYGB) are more preferred in patients with higher body weights (Table 1).

The preoperative hypocalcemia rates were 14% in group 1 and 19.1% in group 2. These rates were not at the level reported in the literature (29%). This difference may be attributed to the advantageous utilization of sunlight in Turkey and the dietary habits of the Turkish people. In the 2nd group with higher BMI, the rate of hypocalcemia was significantly higher than in the 1st group (14% vs. 19.1%). This finding supports the

claim that weight gain increases hypocalcemia. Asghari et al. (16) in their study of 2008 obese patients living in Tehran, they found that weight gain negatively affected blood Ca levels.

Postoperative hypocalcemia rates were higher in both groups. This finding is consistent with the literature (12,13,16,22). It has been reported that decreased Ca^{+2} intake due to restriction of food intake (LSG) and decreased Ca^{+2} absorption due to malabsorption methods (RYGB), increased adipose tissue loss due to weight loss, and increased vitamin D loss due to this loss are effective in the development of postoperative hypocalcemia (18,20). In this regard, Costa et al. (12) they made similar statements, stating that a 10% weight loss may cause a 1-2% loss in bone mass and that the reason for the loss in bone mass is both the loss in dry body weight and inadequate Ca absorption due to bariatric interventions.

In our study, no mineral supplementation was administered to patients in the first 3-6 months postoperatively. However, vitamin D and mineral supplementation (Ca^{+2}) was administered after 6 months. This supplementation prevented the increase in hypocalcemia and partially corrected it compared with the previous months, but could not bring it to normal levels (Table 2). This finding is consistent with the literature (12,20,23,24).

Moore and Sherman (23) They reported that vitamin D insufficiency developed in patients who underwent LSG and RYGB, and vitamin D insufficiency was reduced in patients who received 2,000 IU vitamin D3 and 1,500 mg Ca citrate daily, but none of the patients reached normal levels. These findings are consistent with our findings.

Muschitz et al. (18) they reported that both LSG and RYGB had a negative effect on bone metabolism and mineral density despite effective weight loss. They gave their patients 16,000 IU vitamin D daily and 1,000 mg Ca mono-citrate daily. They stated that although this application decreased vitamin D deficiency, it did not result in complete recovery.

In both groups, P (phosphorus) values were inversely proportional to the changes in Ca^{+2} levels and P levels increased inversely proportional to the decrease in postoperative Ca^{+2} levels (Table 2). Although these findings seemed to contradict physiological functioning, they were in accordance with the literature (12,20,23,24).

Normally, Ca^{+2} and phosphates interact together during bone mineralization. Vitamin D increases blood levels of both Ca^{+2} and phosphates. However, PTH increases blood Ca levels, whereas phosphates are excreted from the kidneys in the urine, leading to a decrease in phosphate levels in the blood (25). The reason for the Ca^{+2} and P discrepancy in our study may be explained by the fact that PTH, which increased in our patients due to hypocalcemia in the pre- and postoperative periods, caused a situation independent of the Ca^{+2} level in the increase or decrease of phosphates. It is possible that low vitamin D levels also contributed to this result.

In our study, PTH levels were found to increase or decrease inversely with Ca^{+2} levels and vitamin D levels (Table 2). These findings are consistent with the physiologic functioning of vitamin D and Ca^{+2} metabolism (25). PTH levels increase to compensate for hypocalcemia. Increased PTH causes an increase in blood Ca and decreases blood P levels by excreting phosphates in the urine (25,26).

Similar to the literature, vitamin D and Ca levels were found to be low in obese patients. These deficiencies are not as low as in western societies. We believe that the reason for this situation may be related to the fact that our country has the opportunity to benefit more from sunlight and the dietary habits of the Turkish people.

The LSG and RYGB methods for weight loss resulted in effective weight loss. Vitamin D and Ca deficiencies increased in parallel with weight loss after surgical interventions. This finding is consistent with the literature.

Vitamin D and Ca supplements were administered starting from the sixth month. Although these supplements partially corrected the patients' vitamin D and Ca deficiency, they could not bring them to normal levels. Similar findings have been reported in other studies.

Study Limitations

There are some limitations to this study. Our study was a two-center, retrospective study, and the results cannot be generalized to the general population. The sample size is small, so studies with more patients are needed.

Conclusion

In light of these data, vitamin D insufficiency and Ca deficiency, which are already present in obese patients, increase even more after bariatric interventions. These deficiencies are believed to increase the risk of osteoporosis. Supplements that correct the current picture are insufficient. We believe that higher doses would be beneficial for the complete resolution of vitamin D insufficiency and Ca deficiency.

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 164, date: 20.05.2022).

Informed Consent: Informed consent was obtained from the patients.

Authorship Contributions: Surgical and Medical Practices - M.E.K.; Concept - Z.A.S.; Design - M.Ş.; Data Collection or Processing - M.Ö.; Analysis or Interpretation - M.E.U., M.Ş.; Literature Search - E.Ş.; Writing - M.Ö., Z.A.S.

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