







The associations of RENAL, PADUA and C-index nephrometry scores with perioperative outcomes and postoperative renal function in minimally invasive partial nephrectomy

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ABSTRACT

Objective: This study aimed to assess the utility of the radius, exophytic/endophytic, nearness, anterior/posterior, location (RENAL); preoperative aspects and dimensions used for an anatomic evaluation (PADUA), and centrality index (C-index) scores for the outcomes of partial nephrectomy (PN).

Material and methods: The patients who underwent PN with contrast-enhanced preoperative imaging from January 2015 to June 2018 were identified. The RENAL, PADUA, and C-index scores were assigned. The correlation between these scoring systems and perioperative and long-term renal functional outcomes were evaluated.

Results: A total of 78 patients were included in the study (58 men and 20 women; age, 58±11.4 years). Median warm ischemia time (WIT), estimated blood loss (EBL), and operation time (OT) were 26 min, 115 mL, and 140 min, respectively. The RENAL score was related to WIT, EBL, and OT ($p<0.001$, $p=0.003$, and $p=0.023$, respectively). The PADUA score was associated with WIT, EBL, and OT ($p<0.001$, $p=0.013$, and $p=0.005$, respectively). The C-index score was correlated with WIT, EBL, and OT ($p<0.001$, $p=0.010$, and $p=0.001$, respectively). The C-index score also correlated with the percentage change in the estimated glomerular filtration rate ($p=0.037$). However, on univariable and multivariable regression analyses, only WIT significantly affected the postoperative estimated glomerular filtration rate reduction.

Conclusion: The RENAL, PADUA, and C-index scores were significantly associated with perioperative outcomes of PN. In addition, the C-index score was correlated with long-term renal functional outcomes.

Keywords: Anterior/posterior; C-index; exophytic/endophytic; location; nearness; nephrometry score; partial nephrectomy; preoperative aspects and dimensions used for an anatomic evaluation; radius.

Introduction

The incidence of small renal masses is increasing, and the cases of renal cell carcinoma (RCC) are being frequently detected incidentally because of the growing use of imaging modalities for unrelated reasons.^[1] Partial nephrectomy (PN) is widely preferred as a nephron-sparing approach for the surgical treatment of clinically localized RCC. Compared with radical nephrectomy (RN), PN demonstrates equivalent oncological outcomes and preserves the renal function.^[2] However, PN is a more challenging procedure to perform than RN, especially in complex renal masses. Therefore, the tumor anatomy and complexity remain the

primary determinant as to which procedure should be performed. Various nephrometry scoring systems have been proposed to provide objective information regarding the anatomical features of renal tumors using cross-sectional imaging. These scoring systems may also assist the surgeon in the surgical decision making and predict the surgical outcomes in addition to facilitating a standardized academic communication. They also allow more meaningful comparisons of surgical series and could be useful to objectify the surgical complexity.

Multiple nephrometry scores have been designed and validated to evaluate the renal masses. The radius, exophytic/endophytic, nearness, anterior/posterior, location (RENAL)

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nephrometry score; preoperative aspects and dimensions used for an anatomic classifications (PADUA) score; and centrality index (C-index) remain the most known and used systems. The RENAL and PADUA scores were described in 2009 and are based on the tumor characteristics, which are summed to provide an overall score.^[3,4] The C-index is a mathematical formula that measures the ratio of the tumor size and the distance from the tumor center to the kidney center.^[5]

Consequently, the proposed nephrometry scores have been successfully validated for predicting the outcomes of PN; however, the results of respective studies are controversial.^[6-9] It remains unclear which of these scores can accurately predict the outcomes of PN. In this study, we aimed to evaluate the role of RENAL, PADUA, and C-index scores in association with perioperative and postoperative renal functional outcomes in a single-center series of patients undergoing robotic-assisted PN (RPN) and laparoscopic PN (LPN).

Material and methods

Study population

After the local institutional review board approval, we retrospectively identified the prospectively maintained database records of 130 patients who underwent LPN or RPN for a suspicious renal mass between January 2015 and June 2018 at our institution. The study protocol was reviewed and approved as a retrospective study by the institutional review board of Antalya Training and Research Hospital (approval number: 2017-194). Informed consent was obtained by all patients when they were enrolled. Of the 130 patients, those who had multiple tumors or solitary kidney, underwent open PN, and those with a follow-up time shorter than 1 year were excluded. Thus, the final study population included 78 patients.

Main Points:

- Various nephrometry scoring systems have been proposed to provide objective information regarding the anatomical features of renal tumors using imaging modalities.
- It remains unclear which of these scores can predict the outcome of partial nephrectomy accurately.
- In this study, we assessed the radius, exophytic/endophytic, nearness, anterior/posterior, location (RENAL); preoperative aspects and dimensions used for an anatomic evaluation (PADUA), and centrality index (C-index) scores for their role in predicting the outcomes of partial nephrectomy.
- Our study revealed that the RENAL, PADUA, and C-index scores were significantly associated with warm ischemia time, estimated blood loss, and operation time.
- The C-index score also correlated with postoperative renal functional change and thus could be promising for future studies.

All patients underwent preoperative imaging with contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). The nephrometry scores were calculated retrospectively by a radiologist who was blinded to the patient characteristics and surgical outcomes. The tumors were classified into low complexity (score 4–6), intermediate complexity (score 7–9), and high complexity (score 10–12) according to the RENAL score. For PADUA classification, the renal masses were divided into low complexity (score 6–7), intermediate complexity (score 8–9), and high complexity (score 10–14). Complexity of the tumors was deemed low if the C-index score was greater than 2.5 and high if the C-index score was lower than 2.5.

All participants included in this study underwent LPN or RPN by 2 surgeons who had extensive LPN and RPN experience. Resection of the tumor was performed with the conventional on-clamp technique. All the procedures were performed with a transperitoneal approach. None of the patients required conversion to open approach.

Acquisition and definition of data

Preoperative demographic data (sex, age, and comorbidities), clinical information (tumor side, clinical tumor size, and RENAL, PADUA, and C-index scores), and perioperative outcomes (operation type, warm ischemia time [WIT], estimated blood loss [EBL], and operation time [OT]) were recorded. Moreover, 3-month postsurgical complications were classified according to the Clavien–Dindo system.^[10]

Renal function was obtained by recording the preoperative and postoperative serum creatinine levels within 12 months of surgery. Preoperative creatinine levels were measured routinely 3–7 days before the surgery. We also calculated estimated glomerular filtration rate (eGFR) using the modification of diet in renal disease formula. In addition, the renal functional outcomes were represented by the absolute change in eGFR (ACE) and the percentage change in eGFR (PCE). The PCE was defined as $[(\text{preoperative eGFR} - \text{postoperative eGFR at 12 months}) / \text{preoperative eGFR}] * 100\%$, whereas the ACE was defined as $\text{preoperative eGFR} - \text{postoperative eGFR at 12 months}$.

The following variables were identified as indicators of the pathological outcome: tumor size, histological subtypes, tumor grade according to the World Health Organization/International Society of Urologic Pathologists grading system, pathological stage according to 2017 tumor nodes metastases (TNM) classification system, and surgical margin status.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences for Windows, Version 23.0 (IBM SPSS

Corp.; Armonk, NY, USA). Fisher's exact test and Pearson's chi-squared analysis were performed for categorical variables. The normality assumptions were controlled by the Shapiro-Wilk test. The differences between the 2 groups were evaluated using Student's t test for normally distributed data or Mann-Whitney U test for nonnormally distributed data. Kruskal-Wallis test was used for the comparison of nonparametric variables between the groups, Bonferroni-Dunn test was used as a post-hoc test for significant cases, and one-way analysis of variance with post-hoc Tukey honestly significant difference test was used for parametric variables. Paired t test was used for parametric comparison of the variables measured before and after the operation. Friedman test with Bonferroni correction was used for nonparametric comparison of the parameters measured at different times. Spearman correlation coefficient was applied to investigate the correlation between the continuous variables. Univariate and multivariate linear regression analyses were performed to determine the association between eGFR percentage change and the study parameters. Data were expressed as n (%), mean±standard

deviation, or median (minimum–maximum) as appropriate. $P<0.05$ was considered statistically significant.

Results

Patients' demographics, perioperative outcomes, and pathological data are summarized in Table 1. The entire cohort aged 58.5 years on median (range, 34–82), with a median clinical tumor size of 3.65 cm. The majority of the patients were men (74.4%). Median WIT, EBL, and OT were 26 min, 115 mL, and 140 min, respectively. The median pathological tumor size was 3.5 cm, and 84.6% (n=66) of the renal masses were RCC. A total of 5 (7.6%) patients had positive surgical margins.

The preoperative median RENAL, PADUA, and C-index scores were 7, 8, and 2.06, respectively. The complexity distribution of nephrometry scores is shown in Table 2. Because only 2 patients were in the high-complexity group for the RENAL score, the

Table 1. Patients' demographics, perioperative outcomes, and pathological results

| Variables | n=78 | | |
|---|--------------|--|------------|
| Age, years, median (min–max) | 58.5 (34–82) | Tubulointerstitial nephritis | 1 (8.3) |
| Sex, n (%) | | Hydatid cyst | 3 (25) |
| Male | 58 (74.4) | Malignant | 66 (84.6) |
| Female | 20 (25.6) | Clear | 41 (62.1) |
| Diabetes, n (%) | 11 (14.1) | Papillary | 14 (21.2) |
| Hypertension, n (%) | 15 (19.2) | Chromophobe | 10 (15.2) |
| Atherosclerosis, n (%) | 12 (15.4) | Cystic | 1 (1.5) |
| Tumor side, n (%) | | Surgical margin, n (%) | |
| Left | 43 (55.1) | Negative | 61 (92.4) |
| Right | 35 (44.9) | Positive | 5 (7.6) |
| Operation type, n (%) | | Pathological stage, n (%) | |
| Robotic | 55 (70.5) | T1a | 38 (57.6) |
| Laparoscopic | 23 (29.5) | T1b | 25 (37.9) |
| Warm ischemia time, min, median (min–max) | 26 (14–48) | T2a | 1 (1.5) |
| Operation time, min, median (min–max) | 140 (80–280) | T3a | 2 (3) |
| Estimated blood loss, mL, median (min–max) | 115 (20–360) | WHO/ISUP tumor grade, n (%) | |
| Clinical tumor size, cm, median (min–max) | 3.65 (1.9–9) | 1 | 11 (16.7) |
| Pathological tumor size, cm, median (min–max) | 3.5 (1–7.2) | 2 | 39 (59.1) |
| Tumor type, n (%) | | 3 | 15 (22.7) |
| Benign | 12 (15.4) | 4 | 1 (1.5) |
| Angiomyolipoma | 4 (33.3) | Hospitalization, day, median (min–max) | 3 (2–7) |
| Chronic pyelonephritis | 1 (8.3) | Complication, n (%) | 9 (11.5) |
| Benign cyst | 1 (8.3) | Follow-up time, months, median (min–max) | 24 (12–54) |
| Oncocytoma | 2 (16.7) | | |

max: maximum; min: minimum; WHO/ISUP: World Health Organization/International Society of Urologic Pathologists

Table 2. Overall nephrometry scores and risk groups

| | n=78 |
|---------------------------|------------------|
| RENAL, median (min–max) | 7 (4–10) |
| RENAL risk, n (%) | |
| Low | 33 (42.3) |
| Intermediate | 43 (55.1) |
| High | 2 (2.6) |
| PADUA, median (min–max) | 8 (6–11) |
| PADUA risk, n (%) | |
| Low | 26 (33.3) |
| Intermediate | 30 (38.5) |
| High | 22 (28.2) |
| C-index, median (min–max) | 2.06 (0.47–6.04) |
| C-index, n (%) | |
| Low | 26 (33.3) |
| High | 52 (66.7) |

C-index: centrality index; max: maximum; min: minimum; PADUA: preoperative aspects and dimensions used for anatomic complexity; RENAL: radius, exophytic/endophytic, nearness, anterior/posterior, location

Table 3. Comparison of preoperative and postoperative renal functional outcomes

| | Total (n=78) |
|--|---------------------|
| Preoperative creatinine, mg/dL | 1.04±0.38 |
| Postoperative first day creatinine, mg/dL | 1.21±0.48 |
| 12 months after surgery creatinine, mg/dL | 1.15±0.75 |
| p | <0.001* |
| Preoperative eGFR, mL/min/1.73 m ² | 78.72±17.76 |
| Postoperative first day eGFR, mL/min/1.73 m ² | 69.18±15.89 |
| First year eGFR, mL/min/1.73 m ² | 73.86±19.54 |
| p | <0.001* |
| eGFR difference | –5.06±8.2 |
| Postoperative first day eGFR % change | –11.66±15.22 |
| First year eGFR % change | –6.81±12.05 |

eGFR: estimated glomerular filtration rate.

intermediate- and high-complexity groups were combined for a more accurate comparison.

The comparison of preoperative and postoperative renal functional outcomes is presented in Table 3. The mean ACE and PCE were –5.06±8.2 and –6.81%±12.05%, respectively. This difference showed statistical significance ($p<0.001$).

Table 4. Association of nephrometry score risk groups with surgical outcomes, pathological results, and renal functional outcomes

| | RENAL | | | PADUA | | | C-index | | |
|--------------------------|--------------|-------------------|--------------|--------------|--------------|----------------|----------------|---------|-------|
| | Low | Intermediate-high | Low | Intermediate | High | Low | High | Low | High |
| | (n=33) | (n=35) | (n=26) | (n=30) | (n=22) | (n=26) | (n=52) | | p |
| Warm ischemia time, min | 23 (14–36) | 28 (17–48) | 22.5 (14–34) | 28 (17–42) | 28 (22–48) | 22.5 (14–38) | 28 (15–48) | 0.001 | |
| Operation time, min | 135 (80–190) | 145 (85–280) | 125 (80–180) | 150 (85–210) | 150 (90–280) | 127.5 (85–220) | 150 (80–280) | 0.008 | |
| Estimated blood loss, mL | 100 (20–310) | 140 (30–360) | 100 (20–310) | 120 (30–360) | 155 (50–300) | 100 (20–310) | 125 (30–360) | 0.074 | |
| Surgical margin | | | | | | | | | |
| Negative | 28 (96.6) | 33 (89.2) | 22 (95.7) | 22 (84.6) | 17 (100) | NA | 21 (91.3) | 40 (93) | 0.999 |
| Positive | 1 (3.4) | 4 (10.8) | 1 (4.3) | 4 (15.4) | 0 (0) | 2 (8.7) | 3 (7) | | |
| eGFR % change | –5 (–55–24) | –8 (–25–23) | –6 (–55–24) | –7 (–40–23) | –7 (–25–14) | –5.5 (–55–24) | –8 (–40–23) | 0.121 | |
| Hospitalization, day | 3 (2–4) | 3 (2–7) | 3 (2–4) | 3 (2–6) | 3 (2–7) | 3 (2–6) | 3 (2–7) | 0.233 | |
| Complication, n (%) | 5 (15.2) | 4 (8.9) | 4 (15.4) | 2 (6.7) | 3 (13.6) | 3 (11.5) | 6 (11.5) | 0.999 | |

C-index: centrality index; eGFR: estimated glomerular filtration rate; PADUA: preoperative aspects and dimensions used for anatomic complexity; RENAL: radius, exophytic/endophytic, nearness, anterior/posterior, location

Table 5. Correlation between the nephrometry scores and the study parameters (n=78)

| | RENAL | | PADUA | | C-index | |
|----------------------|--------|---------|--------|---------|---------|---------|
| | r | p | r | p | r | p |
| Warm ischemia time | 0.447 | <0.001* | 0.503 | <0.001* | -0.476 | <0.001* |
| Operation time | 0.258 | 0.023* | 0.315 | 0.005* | -0.369 | 0.001* |
| Estimated blood loss | 0.333 | 0.003* | 0.279 | 0.013* | -0.290 | 0.010* |
| eGFR % change | -0.209 | 0.066 | -0.173 | 0.131 | 0.237 | 0.037* |
| Hospitalization | 0.191 | 0.094 | 0.046 | 0.691 | -0.020 | 0.859 |

C-index: centrality index; eGFR: estimated glomerular filtration rate; PADUA: preoperative aspects and dimensions used for anatomic complexity; RENAL: radius, exophytic/endophytic, nearness, anterior/posterior, location

Table 6. Correlation of PCE with the study parameters in univariate and multivariate regression analyses

| | Univariate | | | Multivariate | | |
|--------------------|------------|--------------|-------|--------------|--------------|--------|
| | β | 95% CI | p | β | 95% CI | p |
| Warm ischemia time | -0.51 | -0.88, -0.13 | 0.010 | -0.609 | -1.2, -0.02 | 0.044* |
| Operation time | -0.05 | -0.12, 0.02 | 0.146 | 0.014 | -0.08, 0.11 | 0.776 |
| Diabetes | -0.01 | -7.87, 7.85 | 0.998 | -1.205 | -9.48, 7.07 | 0.772 |
| Hypertension | -2.55 | -9.46, 4.37 | 0.465 | -0.579 | -8.12, 6.97 | 0.879 |
| Atherosclerosis | -3.08 | -10.63, 4.46 | 0.418 | -2.738 | -11.02, 5.55 | 0.512 |
| RENAL score | -0.99 | -2.75, 0.77 | 0.267 | -0.874 | -3.9, 2.15 | 0.566 |
| PADUA score | -0.75 | -2.51, 1 | 0.398 | 0.498 | -2.67, 3.66 | 0.755 |
| C-index | 0.52 | -1.98, 3.02 | 0.679 | -1.419 | -4.85, 2.01 | 0.412 |

C-index: centrality index; CI: confidence interval; PADUA: preoperative aspects and dimensions used for anatomic complexity; PCE: percentage change in estimated glomerular filtration rate; RENAL: radius, exophytic/endophytic, nearness, anterior/posterior, location

Table 4 shows the perioperative outcomes, surgical margin status, renal functional outcome, and complications stratified according to all the 3 nephrometry scores. Each scoring system was significantly associated with WIT ($p=0.001$). With the PADUA and C-index scores, we found significant associations between the risk groups and OT ($p=0.013$ and $p=0.008$). Furthermore, the RENAL score was associated with a higher EBL ($p=0.005$). However, no significant correlation was observed between all the scores and surgical margin status, PCE, hospitalization, and complications ($p>0.005$).

The Spearman correlation analysis showed that all the 3 nephrometry scores were significantly associated with WIT, OT, and EBL (Table 5). The C-index score also correlated with PCE.

On univariable and multivariable regression analyses, only WIT significantly affected the postoperative eGFR reduction (Table 6). In the multivariate analysis, none of the nephrometry scores could predict PCE.

Discussion

Nephrometry scores have been designed to estimate the complexity of renal masses suitable for PN and consequently assist

in decision-making and patient-counseling processes. Moreover, many studies have investigated their use as predictors of perioperative outcomes. In this study, we assessed the associations of RENAL, PADUA, and C-index scores with the outcomes of PN. Our study revealed that all the 3 scores were associated with WIT, OT, and EBL. The C-index score correlated with the postoperative renal functional change. However, this difference did not show a statistical significance in the univariate and multivariate analyses.

PN has become more preferable in the treatment of renal masses after the oncological outcomes of PN and RN have been shown to be similar.^[2] PN is technically a more difficult procedure and associated with a higher risk of complications than RN. Many investigators have evaluated the ability of the nephrometry scores to predict the surgical complications.^[11-15] Kriegmair et al.^[11] found that the RENAL and PADUA scores were significantly associated with severe complications in 305 patients treated with open PN. A previous study also showed that the PADUA score predicted surgical complications.^[12] Conversely, some authors failed to identify a correlation between the nephrometry scores and complications.^[13-15] In our study, there was no significant association between the RENAL, PADUA, and

C-index scores and the incidence of complications. Contradictory results in terms of complications can be attributed to the surgeon's experience, hilar anatomy in each patient, tumor characteristics, the patient's age, and comorbid diseases. We believe that the experience of the surgeon is more important than the tumor characteristics in predicting the complications.

Another controversial issue concerns the ability of the nephrometry scores to estimate the perioperative outcomes. In a single-center Canadian cohort, although the RENAL and PADUA scores were associated with WIT, the C-index score failed to show the same correlation.^[16] Borgmann et al.^[7] also found that the RENAL and PADUA scores correlated with WIT, OT, and length of stay (LOS); the C-index score was only associated with WIT. In a study with 162 patients, all the 3 nephrometry scores were able to predict WIT. There was no significant relationship between the nephrometry scores and OT and EBL.^[9] In the study by Sugiura et al.^[17], the RENAL and C-index scores were useful for predicting WIT and OT, and the C-index score was also associated with EBL. Corradi et al.^[18] reporting data from 283 patients who underwent RPN, found a significant correlation between the RENAL, PADUA, and C-index scores and WIT, EBL, and LOS. Other investigators have published contradictory results. None of the RENAL, PADUA, and C-index scores were able to estimate the perioperative outcomes.^[8,13] Most of the previous studies included patients who underwent open PN, LPN, and RPN. Different types of operations may cause the results to be contradictory. Variables depending on the patients may also lead to different results. For example, in a study investigating the role of obesity in RPN, higher EBL longer WIT and OT were observed in obese patients.^[19] Cacciamani et al.^[20] performed a systematic review and meta-analysis including the patients treated by RPN. The RENAL score was able to predict OT, WIT, and EBL. However, it could not predict LOS, major complications, and renal function. A recent meta-analysis showed that the RENAL and PADUA scores were predictors of WIT and overall complications.^[21] The RENAL score was also an independent predictor of increase in eGFR.

Although the purpose of PN is to maintain the renal functions as much as possible, there may be a reduction in the renal function owing to irreversible ischemic damage and vascularized nephron loss. A 10% of total renal function loss after PN for patients with a two-kidney model.^[22] Our results showed that the mean PCE was 6.81%. Previous studies on this topic suggested that WIT was the strongest predictor of renal functional outcomes.^[23] However, in later studies, most nephrons recovered their preoperative function after on-clamp PN as long as prolonged warm ischemia was avoided.^[24] The investigators concluded that the quality and quantity of nephrons preserved after PN were the key predictors in the long-term renal function.^[25] On the basis of this, Lee et al.^[26] calculated the CT-based renal cortical volume (RCV) after PN. They evaluated the predictive value of the nephrometry scores in RCV preservation. On multivariate

regression analysis, the PADUA and C-index scores independently affected the percentage reduction in RCV.

Different results were obtained in studies investigating the association between the nephrometry scores and renal functional outcomes.^[9,11,13,15,17,27] In this study, the C-index score outperformed the RENAL and PADUA scores in predicting PCE. However, this result was not obtained in univariate and multivariate analyses. The reason of insignificance can be attributed to the number of patients. Several authors reported renal functions according to the creatinine values on the first postoperative day.^[13,15] These studies are insufficient to demonstrate the long-term renal functions. Spaliviero et al.^[27] analyzed the correlation between the nephrometry scores and PCE at 6 weeks after surgery. Only the C-index score was a significant predictor of PCE. Another study evaluating the nephrometry scoring systems for predicting PCE at 3 months after PN showed that the RENAL and C-index scores were significantly associated with reduction of eGFR^[17]; however, other investigators failed to identify such a link.^[9,11] Several reasons can be attributed to these contradictory observations. eGFR calculations based on serum creatinine level show global renal function. However, compensatory hypertrophy of the contralateral kidney could be observed after PN.^[28] Wang et al.^[29] aimed to evaluate the correlation between the RENAL, PADUA, and C-index scores and the renal functional outcomes of the operated kidney by assessing the radioisotope scans. The C-index score independently affected the percentage change in effective the renal plasma flow in multivariate analysis. Similarly, Kwon et al.^[30] evaluated the associations between the nephrometry scores and eGFR using diethylene triamine penta-acetic acid. The RENAL and C-index scores were significantly predictive of eGFR reduction.

Our study had some limitations. First, we collected our data prospectively but analyzed retrospectively. Second, the cohort was relatively small, although the follow-up period was sufficiently long. Finally, the nephrometry scores were calculated by a single radiologist; therefore, interobserver variability could not be assessed.

In conclusion, our study suggests that the RENAL, PADUA, and C-index scores were associated with WIT, OT, and EBL. Furthermore, C-index had a correlation with postoperative renal functional change. The C-index method provides a continuous index that reflects the tumor size and the tumor centrality. Lower scores are linked to larger and parahilar tumors. Because the patients who underwent PN with lower C-index scores could be associated with greater parenchymal loss. Larger and prospective studies are needed to evaluate the relationship between C-index and renal functional outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Antalya Training and Research Hospital (Approval number: 2017-194).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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