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Original Research

A Comparison of Oncologic Outcomes after Nephrectomy in Kidney Cancer Patients with and without Preoperative Renal Mass Biopsy

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Abstract

Objectives: The objective of this study is to examine the safety of percutaneous renal mass biopsy and compare the oncological outcomes between patients who had a renal biopsy prior to nephrectomy procedures and those who did not have a biopsy.

Methods: We evaluated a total of 145 patients who underwent nephrectomy for renal cancer between January 2017 and January 2021. Based on the pretreatment percutaneous renal mass biopsy, we categorized the patients into two groups: the biopsy (-) group and the biopsy (+) group. We performed a comparative analysis of the radiologic and histological characteristics of the tumors in all the groups. We also conducted an examination of the surgical margin outcomes in cases of partial nephrectomy between the two groups. In addition, we did an analysis of the overall survival (OS), recurrence-free survival (RFS), metastasis-free survival (MFS), and disease-free survival (DFS) between each group.

Results: Out of 145 patients meeting inclusion criteria, we analyzed 119 cases. The mean age and tumor diameter were 56.75±11.71 years and 53.77±23.99 mm, respectively. Operative time averaged 176.87±56.46 minutes, with a mean follow-up of 25.67±14.27 months (range: 8–60 months). Partial nephrectomy rates were 35.41% (biopsy (-)) and 43.47% (biopsy (+)), with left kidney tumors in 46/96 (biopsy (-)) and 16/23 (biopsy (+)) cases, respectively. Cystic and exophytic tumors varied significantly between groups (p=0.01 and p=0.03). During follow-up, 16 deaths occurred. Mean overall survival (OS) was 51.38±2.26 months. We noted local recurrence and metastatic progression in 4 and 7 patients, respectively, with lung metastases in all cases. RFS, MFS and DFS times averaged 57.94±1.00, 54.75±1.67, and 53.83±1.75 months, respectively. The biopsy (+) group showed a higher prevalence of papillary and chromophobe RCC subtypes. Pathological parameters and surgical outcomes were comparable between groups. OS, RFS, MFS, and DFS times did not significantly differ (p>0.05).

Conclusion: According to our findings, a percutaneous renal mass biopsy is a safe procedure. It can aid in the diagnostic evaluation of suspected renal masses and mitigate any adverse effects on oncological outcomes. Our opinion is that patients with suspected renal cancer can safely and successfully use routine percutaneous renal mass biopsy.

Keywords: Diagnosis, image-guided biopsy, kidney, renal cell carcinoma, safety

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Radiologic imaging is the primary diagnostic procedure for renal masses in use today. We use specific radiological criteria with computed tomography (CT) and magnetic resonance (MR) for renal masses to evaluate their benign or malignant characteristics.

Patients with suspected renal masses who are not suitable for surgery or have unresectable renal cancer often undergo renal mass biopsy techniques.[1] However, not all renal masses are malignant, and the majority still receive diagnosis and treatment based solely on radiologic imaging findings. This approach sometimes results in potential overtreatment.[2] Because of the overtreatment potential, percutaneous renal mass biopsy is now increasingly used to differentiate between benign and malignant masses.[1,2]

The most significant issue surrounding the percutaneous renal mass biopsy stems from historical concerns about the procedure's safety and efficacy.[3,4] These concerns have led to the acceptance of the percutaneous renal mass biopsy as unnecessary and potentially dangerous.[5] The safety concern surrounding the percutaneous renal mass biopsy remains ongoing, and there is currently no comparative study available in the literature on this topic. We investigated the safety of the percutaneous renal mass biopsy by comparing the cancer outcomes of patients who had a renal biopsy before a nephrectomy to those of patients who had never had a biopsy before.

Methods

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. We conducted a retrospective review of our institutional data, which included clinical notes, radiology, laboratory, and pathology data. Our hospital's clinical research ethics committee approved the study under approval code 2022/11/15/036. We also obtained an informed consent form from the participants. A total of 145 patients who underwent nephrectomy procedures for renal cancer between January 2017 and January 2021 were evaluated. We excluded patients who had a history of metastatic disease, concomitant malignancies other than renal cancer, or had undergone a nephrectomy for renal cancer. Additionally, patients with renal-collecting system cancers were excluded.

We grouped patients based on the pretreatment percutaneous renal mass biopsy. Patients who had no biopsy protocol prior to nephrectomy were named the biopsy (-) group, whereas patients who had it prior to nephrectomy were named the biopsy (+) group. An experienced interventional radiologist performed all biopsy protocols using an 18-gauge tru-cut biopsy needle, guided by ultrasonography (USG) imaging, and applied local anesthesia with 1% lidocaine prior to the procedure. We used a separate tru-cut sampling technique to obtain up to four cores from each kidney mass. Post-biopsy images were not routinely obtained, and patients were observed closely and hemodynamically monitored for three hours. We performed an open or laparoscopic nephrectomy under general anesthesia. All biopsy and surgical specimens were immediately fixed in 10% formalin and underwent routine pathological processing. An experienced genito-urinary pathologist (S.O.) reviewed all biopsies. The primary techniques preferred are hematoxylin and eosin staining. Pathologists evaluate and report renal tumor specimens using the WHO TNM classification system and the Fuhrman nuclear grading system.[6]

Cross-sectional imaging studies assessed the kidney masses' characteristics, including size, side, polarity, localization, and exophytic or endophytic character. We compared the radiologic and histopathological characteristics of the tumors between the groups. The status of the surgical margin results after partial nephrectomy cases was also compared between the groups. The follow-up schedule was physical examination, blood biochemistry, and radiologic imaging with contrast-enhanced abdominal computerized tomography every 3-6 months in 2 years, 6–12 months in 2–5 years, according to the individual patient and tumor characteristics. The last survival follow-up date was December 1, 2021. We extracted incidences of local recurrence and metastasis from the data during the follow-up and compared them between the groups. Overall survival (OS), recurrence-free survival (RFS), and metastasis-free survival (MFS) were also compared between the groups. The absence of any local recurrence or metastasis determined the disease-free status, and we also compared the disease-free survival (DFS) between the groups. We calculated OS as the time from surgery to death or the last follow-up, while we calculated RFS and MFS as the times from surgery to local recurrence and metastasis, respectively, or the last follow-up. The determination of DFS took place from the time of surgery until the occurrence of local recurrence and/or metastasis or until the last follow-up.

Statistical Analysis

The statistical analysis was performed using the SPSS Version 22.0 statistical software package (IBM SPSS Inc., Chicago, IL). We evaluated data distributions and tests of normality using the Shapiro-Wilk test. Descriptive statistical methods (mean±standard deviation, median±interquartile range, and percentages) were used to express the data. Normally distributed data between the groups were compared using an independent t-test, while a chi-square test was applied for the comparison of nonparametric categori-

cal variables. Additionally, survival analysis and curves for the groups were generated using the Kaplan-Meier method and compared using the log-rank test. The analyses included both univariate and multivariate logistic regression to assess the associations between demographic and clinical variables and the outcome. Differences were considered significant at a two-sided $p<0.05$ with a 95% confidence interval.

Results

We investigated a total of 119 cases out of 145 patients who met the inclusion criteria. We performed surgery using open and laparoscopic approaches in 47 and 72 patients, respectively. Within the biopsy (-) group, open and laparoscopic techniques were utilized in 7 and 40 patients, while in the biopsy (+) group, these approaches were employed in 16 and 56 patients, respectively. The mean age and the mean tumor diameter were 56.75±11.71 years and 53.77±23.99 mm, respectively. The mean operative time was 176.87±56.46 min. The mean follow-up time was 25.67±14.27 months, with an 8–60 month interval. Table 1 displays the mean age, tumor diameter, operative time, and mean follow-up time for the biopsy (-) and biopsy (+) groups. The median hospital stay was 3±3 days. Out of 119 patients, 47 (39.5%) were female and 72 (60.5%) were male. A total of 51 (42.9%) patients had comorbidities, and 25 (21%) of them had multiple comorbid disorders. The prevalence of any and multiple comorbidities was similar between the biopsy (-) and biopsy (+) groups (40/96 vs. 11/23, p=0.36, and 20/96 vs. 5/23, p=0.53, respectively). Partial nephrectomy was performed for 34 (35.41%) and for 10 (43.47%) cases in the biopsy (-) and biopsy (+) groups, respectively (p=0.06). The tumor was left kidney in 46/96 cases and in 16/23 cases in the biopsy (-) and biopsy (+) groups, respectively (p=0.14). The numbers of cystic and exophytic tumors were 3/23 vs. 33/96 and 12/23 vs. 23/96 in the biopsy (-) and biopsy (+) groups, respectively (p=0.01 and p=0.03, respectively). Table 2 provides detailed information about the anatomical tumor characteristics and pathological tumor characteristics between the groups.

During the follow-up, 16 patients died. The mean OS time was 51.38±2.26 months (95% CI: 46.94-55.81). During the follow-up, four patients and seven patients demonstrated local recurrence and metastatic progression, respectively. Partial nephrectomy cases showed local recurrences, and all metastases were in the lungs. The mean RFS time was determined to be 57.94±1.00 months (95% CI: 55.96–59.17). The mean MFS time was determined to be 54.75±1.67 months (95% CI: 51.47–58.02). The mean DFS time was 53.83±1.75 months (95% CI: 50.38–57.27).

According to the tumor subtypes, there was a significant difference between the groups. In the biopsy (+) group, the prevalence of papillary and chromophobe RCC subtypes was significantly higher. However, the groups were similar in terms of pathological parameters such as pT stage, tumor grade, lymphovascular invasion, and variant differentiation (Table 2). The status of the positive surgical margin, as well as the incidence of local recurrence and metastatic progression, was similar between the groups (Table 3).

Table 4 presents a comparison of comorbidities between patients with negative biopsy results (biopsy (-) group, n=96) and those with positive biopsy results (biopsy (+) group, n=23). A significantly higher proportion of patients in the biopsy (+) group had diabetes mellitus (91.3%) compared to the biopsy (-) group (25.8%), a difference that was statistically significant (p=0.02). However, other comorbid conditions, including hypertension, coronary artery disease (CAD), chronic kidney disease (CKD), and the presence of multiple comorbidities, did not show significant differences between the groups. For hypertension, 43.7% of patients in the biopsy (-) group and 39.1% in the biopsy (+) group had the condition (p=0.43). We observed CAD in 17.4% of the biopsy (+) group compared to 9.4% of the biopsy (-) group, but this difference was not statistically significant (p=0.22). CKD prevalence was 4.3% in the biopsy (+) group and 2.1% in the biopsy (-) group (p=0.47). Similarly, the occurrence of multiple comorbidities was comparable, with 21.7% in the biopsy (+) group and 20.8% in the biopsy (-) group (p=0.56). While diabetes mellitus emerged as significantly more prevalent in the biopsy (+) group, the rates of other comorbidities did not differ significantly between the groups.

Table 1. The mean age, tumor diameter, and operative time, and mean follow-up time for biopsy - and biopsy + groups

	Biopsy (-) group (n=96)	Biopsy (+) group (n=23)	p
Age (Year, Mean±SD)	56.87±11.70	62.91±16.15	0.04*
Tumor diameter (mm, Mean±SD)	54.05±29.96	37.26±24.04	0.01*
Operative time (min., Mean±SD)	176.45±35.46	178.66±43.17	0.06*
Mean follow-up (Month, Mean±SD)	25.67±14.27	21.60±14.42	0.22*

SD: Standard deviation, *: Independent t test.

Table 2. Detailed information about the anatomical tumor characteristics and pathological tumor characteristics between the groups

	Superior pole (n=38)	Middle pole (n=51)	Lower pole (n=26)	Whole kidney (n=4)	p
Biopsy (-) group, n (%)	31 (32.3)	41 (42.7)	20 (20.8)	4 (4.2)	0.84
Biopsy (+) group, n (%)	7 (30.4)	10 (43.5)	6 (26.1)	0 (0)	
	Anterior (n=31)	**Medial (n=49)**	**Posterior (n=39)**		
Biopsy (-) group, n (%)	24 (25)	38 (39.6)	34 (35.4)		0.77
Biopsy (+) group, n (%)	7 (30.4)	11 (47.8)	5 (21.8)		
	Clear cell (n=95)	**Papillary (n=15)**	**Chromophobe (n=9)**		
Biopsy (-) group, n (%)	84 (87.5)	7 (7.3)	5 (5.2)		0.001
Biopsy (+) group, n (%)	11 (47.8)	8 (34.8)	4 (17.4)		
	pT1 (n=80)	**pT2 (n=16)**	**pT3 (n=21)**	**pT4 (n=2)**	
Biopsy (-) group, n (%)	61 (63.5)	15 (15.6)	18 (18.8)	2 (2.1)	0.31
Biopsy (+) group, n (%)	19 (82.7)	1 (4.3)	3, (13.0)	0 (0)	
	Grade 1 (n=10)	**Grade 2 (n=59)**	**Grade 3 (n=38)**	**Grade 4 (n=12)**	
Biopsy (-) group, n (%)	7 (7.3)	49 (51.0)	30 (31.3)	10 (10.4)	0.78
Biopsy (+) group, n (%)	3 (13.0)	10 (43.5)	8 (34.8)	2 (8.7)	
	LVI - (n=89)	**LVI + (n=30)**			
Biopsy (-) group, n (%)	70 (71.9)	26 (27.1)			0.24
Biopsy (+) group, n (%)	19 (82.6)	4 (17.4)			
	VD - (n=108)	**VD + (n=11)**			
Biopsy (-) group, n (%)	86 (89.6)	10 (10.4)			0.33
Biopsy (+) group, n (%)	22 (95.7)	1 (4.3)			

LVI: Lymphovascular invasion; VD: Variant differentiation.

Table 3. Status of positive surgical margin and incidence of local recurrence and metastatic progression in the groups

	Surgical margin (-) (n=35)	Surgical margin (+) (n=12)	p
Biopsy (-) group, n (%)	27 (75.0)	9 (25.0)	
Biopsy (+) group, n (%)	8 (72.7)	3 (27.3)	0.60
	Local recurrence (-) (n=115)	**Local recurrence (+) (n=4)**	
Biopsy (-) group, n (%)	93 (96.8)	3 (3.2)	
Biopsy (+) group, n (%)	22 (95.7)	1 (4.3)	0.49
	Metastasis (-) (n=110)	**Metastasis (+) (n=9)**	
Biopsy (-) group, n (%)	89 (92.7)	7 (7.3)	
Biopsy (+) group, n (%)	21 (91.3)	2 (8.7)	0.91

Table 4. Incidences of comorbid disease in the groups

	Biopsy (-) group (n=96)	Biopsy (+) group (n=23)	p
Diabetes Mellitus			
Yes, n (%)	30 (5.8)	21 (91.3)	0.02
No, n (%)	66 (70.2)	2 (8.7)	
Hypertension			
Yes, n (%)	42 (43.7)	9 (39.1)	0.43
No, n (%)	54 (56.3)	14 (60.9)	
Coronary Artery Disease			
Yes, n (%)	9 (9.4)	4 (17.4)	0.22
No, n (%)	87 (90.6)	19 (82.6)	
Chronic Kidney Disease			
Yes, n (%)	2 (2.1)	1 (4.3)	0.47
No, n (%)	94 (97.9)	22 (95.7)	
Multiple Comorbidities			
Yes, n (%)	20 (20.8)	5 (21.7)	0.56
No, n (%)	76 (79.2)	18 (78.3)	

Table 5. Factors affecting surgical approaches in nephrectomy procedures

	Univariate Analysis			Multivariate Analysis		
	Exp B	95 CI	p	Exp B	95 CI	p
Age	0.925	0.89-0.96	<0.001	1.059	0.931-1.203	0.38
Gender	0.81	0.383-1.714	0.58	1.345	0.55-3.288	0.51
Comorbidity	0.567	0.267-1.204	0.13	0.673	0.276-1.638	0.38
Mass Diameter	0.963	0.947-0.98	<0.001	0.934	0.868-1.005	0.06
pT Stage	0.723	0.574-0.91	0.006	2.109	0.202-22.01	0.53

Table 5 presents the results of the univariate and multivariate analyses. In the univariate analysis, age (Exp B=0.925, p<0.001) and mass diameter (Exp B=0.963, p<0.001) were found to be significantly linked to the outcome. This means that getting older and having a bigger mass diameter both make the odds of the dependent variable lower. Conversely, gender, comorbidity, and the pT stage did not demonstrate significant associations. In the multivariate analysis, however, age (Exp B=1.059, p=0.38) and mass diameter (Exp B=0.934, p=0.06) lost their significance. This means that these variables do not predict the outcome on their own when other variables are taken into account. Overall, the findings highlight the importance of age and mass diameter in the initial analysis while emphasizing the need for further investigation of their roles within the context of the studied variables.

OS, RFS, MFS, and DFS times were similar between the groups. OS times were 43.48±5.88 months (95% CI: 40.36-46.59) vs. 57.23±6.61 months (95% CI: 52.01-59.44) for biopsy (-) and biopsy (+) groups, respectively (p=0.22). RFS times were 48.52±0.80 months (95% CI: 46.89-50.16) vs. 57.54±2.39 months (95% CI: 52.84-62.24) for biopsy (-) and biopsy (+) groups, respectively (p=0.79). MFS times were 46.74±1.17 months (95% CI: 44.44-49.04) vs. 53.27±4.34 months (95% CI: 51.47-58.02) for biopsy (-) and biopsy (+) groups, respectively (p=0.65) and DFS times were 46.30±1.23 months (95% CI: 43.87-48.73) vs. 51.12±4.65 months (95% CI: 42.00-54.24) for biopsy (-) and biopsy (+) groups, respectively (p=0.30). Figure 1 provides the survival graphs.

It should be noted that while we collected extensive data regarding various patient demographics and clinical outcomes, body mass index (BMI) information was not consistently recorded in our retrospective dataset. This limitation may hinder a comprehensive understanding of the results, as BMI is a significant factor that can influence both prognosis and treatment outcomes in patients with renal cancer.

Discussion

With advanced imaging modalities, the incidence of renal masses has increased. In this regard, the number of treated patients with renal masses has increased recently.[7,8] However, surgical resection is still the main treatment approach for renal masses suspected of RCC. Although the number of treated cases with RCC has increased over time, the disease's mortality remains relatively stable, suggesting that RCC is overdiagnosed and overtreated.[8,9] In the literature, some of the final pathology results revealed benign diseases after nephrectomy procedures for suspected kidney masses. The reported benign final pathological findings range from 8.1% to 27.5% after partial nephrectomies.[10,11] In a study with a large sample size, the number of benign final pathologic diagnoses was 5588 among the 18,060 patients, and the overall prevalence was 30.9%.[12] Therefore, percutaneous renal mass biopsy procedures have become

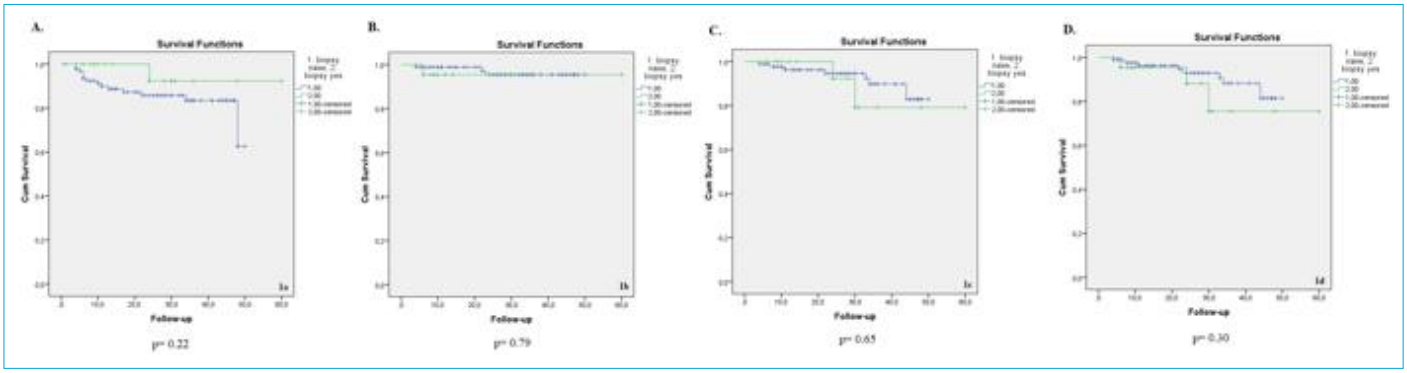

Figure 1. Survival graphs for Overall Survival **(a)**, Recurrence Free Survival **(b)**, Metastasis Free Survival **(c)**, and Disease Free Survival **(d)**.

an important step in avoiding unnecessary nephrectomies.

Percutaneous renal mass biopsy has considerable diagnostic success, with a diagnostic rate of 92% and sensitivity of 94%.[13,14] We rarely see procedure-associated complications, with the rates of minor and major ones being less than 5% and 1%, respectively.[15] On the other hand, the most worrying adverse effect of PRB is the probability of tumor seeding. However, reports indicate that the incidence of tumor seeding is less than 0.01% and only occurs in a few cases.[16] Additionally, several reports asserted that the increase in modern biopsy techniques during the procedure did not result in any cases of tumor seeding.[17] In the present study, we did not detect any procedure-associated complications or tumor seeding at an early or late period during the follow-up. However, the literature about the oncological outcomes of patients who underwent the procedure prior to nephrectomy procedures is still unclear. To our knowledge, no study has examined the incidence of positive surgical margins following partial nephrectomy, as well as the rates of local recurrence and metastasis following nephrectomies for these patients. The present study is the first to investigate and compare the oncological outcomes of those patients with biopsy-naive RCC. We discovered that positive surgical margins were present in 27.3% of patients who underwent renal mass biopsy prior to partial nephrectomies, in contrast to the reported 25% of patients who had not undergone renal mass biopsy. However, the difference was not statistically significant. Our findings revealed that OS, RFS, MFS, and DFS times were similar between the groups. OS times were 43.48±5.88 months (95% CI: 40.36-46.59) vs. 57.23±6.61 months (95% CI: 52.01-59.44) for biopsy (-) and biopsy (+) groups, respectively (p=0.22). RFS times were 48.52±0.80 months (95% CI: 46.89-50.16) vs. 57.54±2.39 months (95% CI: 52.84-62.24) for biopsy (-) and biopsy (+) groups, respectively (p=0.79). MFS times were 46.74±1.17 months (95% CI: 44.44-49.04) vs. 53.27±4.34 months (95% CI: 51.47-58.02) for biopsy (-) and biopsy (+) groups, respectively (p=0.65) and DFS times were 46.30±1.23 months (95% CI: 43.87-48.73) vs. 51.12±4.65 months (95% CI: 42.00-54.24) for biopsy (-) and biopsy (+) groups, respectively (p=0.30). The literature reports a 5-7% incidence of local or systemic recurrence after nephrectomy cases for RCC.[18] RCC occurs primarily in the lungs and bones. Each site has a different time to recur. For example, in patients with pT2 disease, the median months to diagnosis of lung and bone metastases are 31 months (range 4–67) and 24 months (range 3–115), respectively.[19] In the present study, our overall local recurrence and metastasis rates were 3.36 percent and 7.56%, respectively. These findings were consistent with the literature. Local recurrence and metastasis rates were 3.2% and 7.3% for the biopsy (-) group and 4.3% and 8.7% for the biopsy (+) group. Between the groups, the rates of local recurrence and metastasis were statistically similar, and mild increases in the biopsy (+) group were not significant. In brief, our results showed that there was no increase in positive surgical margin status or local or distant relapse with percutaneous renal mass biopsy after nephrectomy.

Our study has several limitations, primarily its retrospective nature and relatively small sample size. Additionally, while the follow-up period was appropriate for capturing most recurrences, it remains relatively short. A significant limitation is the absence of body mass index (BMI) data in our records, which could affect the interpretation of the outcomes, as BMI is an important factor influencing prognosis in renal cancer patients. However, a key strength of this study is that it includes a safety analysis and, for the first time in the literature, compares oncological outcomes between patients who underwent percutaneous renal mass biopsy and those who were biopsy-naive.

Conclusion

Concerns about safety, diagnostic accuracy, and the belief that biopsy results won't change management decisions have historically criticized the role of percutaneous renal mass biopsy. However, according to our findings, a percutaneous renal mass biopsy is a safe procedure. It can aid in the diagnostic evaluation of suspected renal masses and has no adverse events in terms of procedure-associated complications or oncological outcomes. We believe that patients with suspected renal cancer can successfully and safely use routine percutaneous renal mass biopsy.

Disclosures

Ethics Committee Approval: This study was approved by the Bagcilar Training and Research Hospital Non-interventional Clinical Research Ethics Committee (date: 16.11.2022, number: 2022/11/15/036).

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