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Medication Adherence and Health-Related Quality of Life in Patients With Breast Cancer Receiving Oral Anticancer Therapy: A Prospective Observational Study

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Abstract

Purpose

This study evaluated medication adherence among patients with breast cancer receiving oral systemic anticancer therapy and examined its associations with sociodemographic, clinical, treatment-related, and health-related quality-of-life characteristics.

Methods

This prospective cross-sectional study included 95 patients receiving aromatase inhibitor-based therapy, tamoxifen-based therapy, or cyclin-dependent kinase 4/6 inhibitor-based combination therapy. Medication adherence and health-related quality of life were assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8) and EORTC QLQ-C30, respectively. MMAS-8 scores of < 6 and ≥ 6 indicated lower and higher adherence. Binary logistic regression was used to identify factors independently associated with higher adherence.

Results

Overall, 33 patients (34.7%) had lower adherence and 62 (65.3%) had higher adherence. Disease duration was longer in the lower-adherence group (median, 4.0 vs. 3.0 years; $p = 0.029$). Adherence differed according to treatment intent ($p = 0.013$), medication group ($p = 0.048$), and alcohol use status ($p = 0.002$). Higher adherence was associated with better global health status and physical, emotional, cognitive, and social functioning and with lower fatigue, pain, dyspnoea, insomnia, and financial difficulties. The median QLQ-C30 Summary Score was higher in the higher-adherence group (80.00 vs. 68.89; $p < 0.001$). In the multivariable analysis of 80 complete cases, each 10-point increase in the Summary Score was associated with higher odds of higher adherence (adjusted odds ratio, 2.389; 95% confidence interval, 1.488–3.837; $p < 0.001$).

Conclusion

Better health-related quality of life was independently associated with higher medication adherence. Concurrent assessment of adherence and quality of life may help identify patients requiring further evaluation and supportive care.

1. Background

Breast cancer remains a major global health burden. According to the most recent global estimates, approximately 2.4 million women were diagnosed with breast cancer, and 694,000 breast cancer-related deaths occurred worldwide in 2024 [1]. Advances in early diagnosis and multimodal treatment have

improved survival, resulting in a growing population of patients who require long-term follow-up and, depending on tumour biology and disease stage, continued systemic therapy. Oral systemic therapies are particularly relevant for patients with hormone receptor-positive breast cancer receiving tamoxifen or aromatase inhibitors in the adjuvant setting and for selected patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced disease receiving endocrine therapy combined with cyclin-dependent kinase 4/6 inhibitors [2].

Despite their clinical benefits, oral anticancer therapies shift much of the responsibility for treatment administration from healthcare professionals to patients. Treatment-related adverse effects, prolonged treatment duration, comorbid conditions, psychological distress, medication beliefs, and difficulties in maintaining regular follow-up may adversely affect treatment adherence and persistence [3–6]. Non-adherence to adjuvant endocrine therapy has been associated with poorer clinical outcomes and increased mortality [3, 7]. In addition, treatment-related symptoms and functional limitations may adversely affect health-related quality of life, which may, in turn, be associated with patients' ability to maintain long-term treatment [8]. Understanding the relationship between medication adherence and quality of life may therefore help identify patients who require additional supportive care during oral anticancer treatment.

This study aimed to evaluate medication adherence among patients with breast cancer receiving oral anticancer therapy and to determine the independent associations of sociodemographic, clinical, and treatment-related characteristics and health-related quality of life with medication adherence.

2. Methods

2.1 Study Design and Participants

This prospective cross-sectional observational study included patients with breast cancer who attended the Oncology Outpatient Clinic of XXX Training and Research Hospital for routine follow-up between February and July 2026. During the six-month recruitment period, patients who met the eligibility criteria were invited to participate.

Patients were eligible if they had a confirmed diagnosis of breast cancer, had been receiving oral systemic anticancer therapy for at least one year, and were able to understand and complete the study questionnaires. Eligible treatments included aromatase inhibitor-based endocrine therapy, tamoxifen-based endocrine therapy, and cyclin-dependent kinase 4/6 (CDK4/6) inhibitor-based combination therapy. Both patients receiving adjuvant treatment and those receiving palliative treatment for metastatic disease were included.

Patients with cognitive or communication impairments or mental or physical conditions that could interfere with questionnaire completion were excluded. Patients receiving concurrent intravenous anticancer treatment were also excluded to minimise the potential effects of intravenous treatment and its associated adverse effects on medication adherence and health-related quality of life.

A total of 95 patients who met the eligibility criteria, agreed to participate, and provided written informed consent were enrolled. Sociodemographic data included age, educational level, place of residence, employment status, marital status, smoking status, and current alcohol use. Clinical and treatment-related data included age at initial diagnosis, disease duration, treatment intent, medication group, current non-cancer medical comorbidities, and current psychiatric disorders.

2.2 Assessment of Medication Adherence

Medication adherence was assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8). The MMAS-8 is a self-reported instrument consisting of seven dichotomous items and one item rated on a five-point response scale. The total score ranges from 0 to 8, with higher scores indicating better medication adherence [9].

The MMAS-8 conventionally classifies medication adherence as low, moderate, or high. However, because of the limited sample size and the small number of participants in some of the conventional adherence categories, participants were classified into two groups for the present analysis. An MMAS-8 score of < 6 was defined as lower medication adherence, whereas a score of ≥ 6 was defined as higher medication adherence. Accordingly, the conventional moderate- and high-adherence categories were combined.

2.3 Assessment of Health-Related Quality of Life

Health-related quality of life was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), a 30-item cancer-specific instrument [10]. The questionnaire comprises a global health status/quality-of-life scale; five functional scales assessing physical, role, emotional, cognitive, and social functioning; three multi-item symptom scales assessing fatigue, nausea and vomiting, and pain; and six single-item measures assessing dyspnoea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties.

The reliability and validity of the Turkish version of the EORTC QLQ-C30 version 3.0 were demonstrated by Cankurtaran et al. [11]. The validity and reliability of the Turkish EORTC QLQ-C30 and its breast cancer-specific module were subsequently supported in patients with breast cancer by Demirci et al. [12].

Raw scores were linearly transformed to a 0–100 scale in accordance with the EORTC QLQ-C30 scoring manual [13]. Higher functional-scale and global health status scores indicate better functioning and quality of life, whereas higher symptom-scale and financial difficulties scores indicate greater symptom burden or financial difficulties.

The EORTC QLQ-C30 Summary Score was calculated as the mean of the five functional scales and eight symptom scales or items after reversing the symptom scores so that higher values consistently represented better outcomes [14]. The global health status/quality-of-life scale and financial difficulties item were not included in the Summary Score.

2.4 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation or median and interquartile range, according to their distribution. Categorical variables were summarised as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test and graphical inspection. Homogeneity of variance was evaluated using Levene's test.

Continuous variables were compared between the medication-adherence groups using Student's independent-samples *t* test or Welch's *t* test when the assumption of equal variances was not met. Non-normally distributed variables were compared using the Mann–Whitney *U* test. Categorical variables were compared using Pearson's chi-square test. Fisher's exact test was used for 2 × 2 tables, and the Fisher–Freeman–Halton exact test was used for larger contingency tables when the expected cell-count assumptions of the chi-square test were not satisfied.

A multivariable binary logistic regression analysis was performed to identify factors independently associated with higher medication adherence. Medication adherence was entered as the dependent variable, with higher adherence coded as 1 and lower adherence as 0. Variables were selected for the multivariable model based on their associations in the univariable analyses. The final model included the EORTC QLQ-C30 Summary Score, current alcohol use, treatment intent, and disease duration. The Summary Score was modelled per 10-point increase.

Adjusted odds ratios and 95% confidence intervals were reported. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test, and model explanatory performance was summarised using Nagelkerke R^2. The regression analysis was based on participants with complete data for all variables included in the model. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.

2.5 Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the **[name of ethics committee]** (approval date: **[date]**; approval number: **[number]**). Written informed consent was obtained from all participants before enrolment.

3. Results

A total of 95 patients were included, of whom 33 (34.7%) were classified as having lower medication adherence and 62 (65.3%) as having higher medication adherence. Patients with lower adherence had a longer disease duration than those with higher adherence (median: 4.0 vs. 3.0 years; p = 0.029). Medication adherence also differed significantly according to treatment setting (p = 0.013), medication group (p = 0.048), and alcohol use status (p = 0.002). No significant between-group differences were observed in age, age at initial diagnosis, educational attainment, place of residence, employment status, marital status, current non-cancer medical comorbidity, current psychiatric disorder, or smoking status.

Table 1
Sociodemographic and clinical characteristics according to medication adherence level

Characteristic	Lower medication adherence (n = 33)	Higher medication adherence (n = 62)	Test statistic	p value
Age, years, mean ± SD	55.88 ± 13.02	58.92 ± 9.57	Welch's t = − 1.182	0.243
Age at initial diagnosis, years, mean ± SD	49.67 ± 12.05	54.37 ± 10.51	t = − 1.974	0.051
Disease duration, years, median (IQR)	4.00 (2.25)	3.00 (2.00)	U = 568.50	**0.029**
Educational attainment, n (%)			FFH = 6.114	0.271
No formal education	3 (9.1)	2 (3.2)		
Literate without formal schooling	1 (3.0)	4 (6.5)		
Primary school	17 (51.5)	34 (54.8)		
High school	8 (24.2)	10 (16.1)		
Higher education	2 (6.1)	11 (17.7)		
Master's/doctoral degree	2 (6.1)	1 (1.6)		
Place of residence, n (%)			FFH = 1.576	0.553
Village/rural area	3 (9.1)	8 (12.9)		
Town/district	29 (87.9)	48 (77.4)		
City/provincial center	1 (3.0)	6 (9.7)		
Employment status, n (%)			χ^2=1.178	0.555
Not employed	17 (51.5)	36 (58.1)		
Employed	9 (27.3)	11 (17.7)		
Retired	7 (21.2)	15 (24.2)		
Marital status, n (%)			FFH = 3.792	0.122
Single	3 (9.1)	1 (1.6)		
Married	18 (54.5)	43 (69.4)		
Divorced/widowed	12 (36.4)	18 (29.0)		

Characteristic	Lower medication adherence (n = 33)	Higher medication adherence (n = 62)	Test statistic	p value
Treatment setting, n (%)			χ^2=6.191	**0.013**
Adjuvant treatment	32 (97.0)	48 (77.4)		
Palliative/metastatic treatment	1 (3.0)	14 (22.6)		
Medication group, n (%)			χ^2=6.091	**0.048**
Aromatase inhibitor-based endocrine therapy	21 (63.6)	26 (41.9)		
Tamoxifen-based endocrine therapy	10 (30.3)	21 (33.9)		
CDK4/6 inhibitor-based combination therapy	2 (6.1)	15 (24.2)		
Presence of a current non-cancer medical comorbidity, n (%)			χ^2<0.001	0.993
No	17 (51.5)	32 (51.6)		
Yes	16 (48.5)	30 (48.4)		
Presence of a current psychiatric disorder, n (%)			χ^2=1.177	0.278
No	24 (72.7)	51 (82.3)		
Yes	9 (27.3)	11 (17.7)		
Smoking status, n (%)			χ^2=0.295	0.863
Never smoker	20 (60.6)	40 (65.6)		
Current smoker	8 (24.2)	12 (19.7)		
Former smoker	5 (15.2)	9 (14.8)		
Alcohol use status, n (%)			FFH = 10.072	**0.002**
Never used alcohol	24 (72.7)	59 (95.2)		
Current alcohol use	8 (24.2)	2 (3.2)		
Former alcohol use	1 (3.0)	1 (1.6)		

Note.Data are presented as mean ± standard deviation, median (interquartile range), or n (%). Percentages are calculated within medication-adherence groups. Disease-duration data were available for 84 participants, and smoking-status data for 94 participants. Current non-cancer medical comorbidity

indicates at least one ongoing medical condition other than breast cancer at the time of assessment. Welch's t-test, Student's independent-samples t-test, Mann–Whitney U test, Pearson's chi-square test, or the Fisher–Freeman–Halton exact test was used, as appropriate. Bold p values indicate statistical significance.

FFH, Fisher–Freeman–Halton exact test; IQR, interquartile range; SD, standard deviation.

Patients with higher medication adherence had significantly higher global health status/quality-of-life and physical, emotional, cognitive, and social functioning scores. Conversely, patients with lower adherence reported significantly greater fatigue, pain, dyspnoea, insomnia, and financial difficulties. No significant between-group differences were observed in role functioning, nausea and vomiting, appetite loss, constipation, or diarrhoea. The median EORTC QLQ-C30 Summary Score was significantly higher in the higher-adherence group than in the lower-adherence group (80.00 vs. 68.89; $p < 0.001$).

Table 2
Comparison of EORTC QLQ-C30 scores according to medication adherence level

EORTC QLQ-C30 scale	Lower medication adherence, median (IQR)	Higher medication adherence, median (IQR)	Mann–Whitney U	p value
Global health status/QoL	41.67 (29.17)	66.67 (33.33)	536.5	**< 0.001**
Functional scales				
Physical functioning	53.33 (31.67)	73.33 (30.00)	661.0	**0.010**
Role functioning	100.00 (33.33)	100.00 (16.67)	844.0	0.110
Emotional functioning	50.00 (50.00)	75.00 (41.67)	459.0	**< 0.001**
Cognitive functioning	50.00 (33.33)	83.33 (33.33)	347.5	**< 0.001**
Social functioning	66.67 (58.33)	100.00 (33.33)	674.0	**0.004**
Symptom scales/items				
Fatigue	55.56 (44.44)	33.33 (16.67)	516.5	**< 0.001**
Nausea and vomiting	0.00 (8.33)	0.00 (16.67)	1020.0	0.975
Pain	50.00 (50.00)	33.33 (33.33)	725.5	**0.018**
Dyspnea	33.33 (66.67)	0.00 (33.33)	721.5	**0.008**
Insomnia	33.33 (83.33)	33.33 (66.67)	753.0	**0.028**
Appetite loss	0.00 (33.33)	0.00 (33.33)	989.0	0.738
Constipation	0.00 (50.00)	0.00 (33.33)	941.5	0.481
Diarrhea	0.00 (33.33)	0.00 (0.00)	877.0	0.219
Financial difficulties	66.67 (66.67)	16.67 (66.67)	599.5	**< 0.001**
QLQ-C30 Summary Score	68.89 (16.24)	80.00 (19.31)	437.0	**< 0.001**

Note. Data are presented as median (interquartile range). Higher scores on the global health status, functional scales, and QLQ-C30 Summary Score indicate better health-related quality of life, whereas higher symptom and financial-difficulty scores indicate greater symptom burden or difficulty. Comparisons were performed using the Mann–Whitney U test. Bold p values indicate statistical significance.

Valid observations varied because of missing data: physical functioning, n = 93; emotional functioning, fatigue, and diarrhea, n = 94; QLQ-C30 Summary Score, n = 91; all other scales, n = 95. IQR, interquartile range; QoL, quality of life.

The multivariable logistic regression analysis included 80 participants with complete data for all variables entered into the model. The overall model was statistically significant ($\chi^2(4) = 31.873$, $p < 0.001$), demonstrated adequate calibration (Hosmer–Lemeshow $p = 0.669$), and explained 45.5% of the variance according to Nagelkerke R^2. Each 10-point increase in the EORTC QLQ-C30 Summary Score was independently associated with more than twofold higher odds of higher medication adherence (adjusted OR = 2.389, 95% CI 1.488–3.837; $p < 0.001$). Current alcohol use, palliative/metastatic treatment, and disease duration were not independently associated with medication adherence after adjustment.

Table 3
Factors associated with higher medication adherence in binary logistic regression analyses

Predictor	B	SE	Wald χ^2	Adjusted OR	95% CI	p value
EORTC QLQ-C30 Summary Score, per 10-point increase	0.871	0.242	12.980	2.389	1.488–3.837	**< 0.001**
Current alcohol use	−1.606	1.054	2.320	0.201	0.025–1.585	0.128
Palliative/metastatic treatment	1.635	1.206	1.838	5.129	0.483–54.491	0.175
Disease duration, per year	−0.164	0.175	0.878	0.849	0.602–1.196	0.349

Note. The dependent variable was higher medication adherence (1), with lower medication adherence (0) as the reference outcome. Adjusted odds ratios were obtained from a single multivariable binary logistic regression model. Reference categories were no current alcohol use and adjuvant treatment. OR, odds ratio; CI, confidence interval; SE, standard error.

4. Discussion

In this prospective cross-sectional study of patients with breast cancer receiving oral systemic anticancer therapy, approximately two-thirds of participants were classified as having higher medication adherence. The principal finding was that the EORTC QLQ-C30 Summary Score remained independently associated with medication adherence in the adjusted analysis. Each 10-point increase in the Summary Score was associated with more than twofold higher odds of higher medication adherence. Patients with higher adherence also reported better global health status and physical, emotional, cognitive, and social functioning, together with lower fatigue, pain, dyspnoea, insomnia, and financial difficulties. These findings indicate that medication adherence is closely associated with patients' overall functional status and symptom burden.

The proportion of participants with higher adherence in our study (65.3%) was similar to the 62.3% adherence rate reported by Koni et al. among patients receiving oral hormonal therapy [15]. Stahlschmidt et al. reported high adherence in 44% of patients, moderate adherence in 54%, and low adherence in 2% [8]. Comparisons between studies should nevertheless be made cautiously because adherence estimates vary according to the measurement instrument, scoring threshold, treatment duration, and clinical setting. In the present study, the conventional moderate- and high-adherence MMAS-8 categories were combined because of the limited sample size. Our higher-adherence category should therefore not be interpreted as equivalent to the conventional high-adherence category. Nevertheless, the finding that more than one-third of participants had lower adherence remains clinically relevant, given the association between endocrine therapy non-adherence and poorer clinical outcomes and increased mortality [7].

Our findings are consistent with previous evidence linking treatment-related experiences and quality of life with medication adherence. Koni et al. found that satisfaction with treatment-related adverse effects and overall treatment satisfaction were associated with adherence [15], whereas Stahlschmidt et al. reported an association between incomplete adherence and systemic treatment-related adverse effects [8]. In the present study, the QLQ-C30 Summary Score remained associated with adherence after adjustment for current alcohol use, treatment intent, and disease duration. Because this score integrates multiple functional and symptom domains, it may reflect the cumulative burden experienced by patients during long-term oral treatment. However, the cross-sectional design does not establish whether poorer quality of life contributes to non-adherence or whether disease- and treatment-related factors simultaneously influence both outcomes.

The scale-level findings provide further clinical context. Patients with lower adherence reported poorer physical, emotional, cognitive, and social functioning and greater fatigue, pain, dyspnoea, and insomnia. Endocrine therapy has previously been associated with persistent impairment in several quality-of-life domains among breast cancer survivors [16]. Treatment-related symptoms and negative perceptions of treatment may disrupt daily routines, reduce motivation, or contribute to intentional dose omission and treatment discontinuation [4, 6]. However, the individual subscale findings should be considered exploratory because multiple comparisons were performed without adjustment for multiplicity.

Financial difficulties were also more pronounced among patients with lower adherence. Although financial difficulties are not included in the QLQ-C30 Summary Score, this finding suggests that practical and socioeconomic burdens may accompany medication-taking difficulties. In contrast, educational attainment, place of residence, employment status, and marital status were not associated with adherence. Conventional sociodemographic variables may therefore fail to capture the financial and practical challenges experienced by individual patients. Nevertheless, because income, insurance coverage, transportation costs, and out-of-pocket treatment expenditure were not directly assessed, the mechanisms underlying this association could not be determined.

Longer disease duration was associated with lower adherence in the unadjusted analysis but not after adjustment. This pattern is consistent with previous evidence indicating that adherence and persistence may decline over the course of long-term endocrine therapy. A systematic review found that mean adherence decreased substantially between the first and fifth years of adjuvant endocrine treatment and identified adverse effects, comorbidity, and depression among the factors associated with poorer adherence [17]. In our study, attenuation of the association after adjustment suggests that disease duration may partly reflect differences in quality of life or other clinical characteristics rather than having an independent association with adherence.

Adherence also differed according to treatment intent and medication group in the unadjusted analyses. Higher adherence was particularly frequent among patients receiving palliative treatment and CDK4/6 inhibitor-based combination therapy. More frequent monitoring, closer contact with oncology professionals, and greater perceived disease severity may have contributed to this pattern. However, the palliative-treatment and CDK4/6 inhibitor subgroups were small, and medication group was closely related to treatment intent. Medication group was therefore not simultaneously included in the adjusted model because the limited subgroup sizes and clinical overlap would have reduced the reliability of the estimates. These findings should not be interpreted as evidence that a particular treatment setting or medication class results in better adherence.

Current alcohol use was associated with adherence in the unadjusted analysis but not in the multivariable model. Only a small number of participants reported current or former alcohol use, resulting in an imprecise estimate and limiting interpretation. No significant associations were observed for age, current medical comorbidity, current psychiatric disorder, or smoking status. Collectively, these findings suggest that adherence assessment should extend beyond readily available demographic and diagnostic characteristics.

From a supportive-care perspective, concurrent assessment of medication adherence and patient-reported quality of life may facilitate a more comprehensive evaluation of patients experiencing difficulties during oral therapy. Patients reporting worsening fatigue, pain, sleep disturbance, functional limitations, or financial difficulties may benefit from further assessment of medication-taking behaviour and potentially modifiable barriers. However, the EORTC QLQ-C30 should not be considered a screening instrument for non-adherence based on the present findings. Whether symptom-directed supportive-care interventions improve medication adherence should be investigated in longitudinal and interventional studies.

Strengths and limitations

This study evaluated medication adherence together with a comprehensive cancer-specific measure of health-related quality of life and included patients receiving different forms of oral systemic treatment in both adjuvant and palliative settings. Nevertheless, several limitations should be acknowledged. First, adherence was assessed using a self-reported instrument and may have been affected by recall and

social-desirability bias. Adherence and quality of life were also measured concurrently using self-report instruments, raising the possibility of common-method bias.

Second, the single-centre design and relatively small sample, particularly within the palliative-treatment and CDK4/6 inhibitor subgroups, limit generalisability and statistical precision. Third, combining the conventional moderate- and high-adherence categories facilitated analysis but reduced comparability with studies using the conventional three-category MMAS-8 classification. Fourth, the cross-sectional assessment precluded determination of temporality or causality.

Fifth, the adjusted analysis was based on 80 participants with complete data and a limited number of lower-adherence outcomes. The estimates should therefore be interpreted cautiously because of possible model instability. Complete-case analysis may also have introduced selection bias if the data were not missing at random. In addition, the multiple QLQ-C30 subscale comparisons were not adjusted for multiplicity and should be considered exploratory. Finally, residual confounding by treatment duration, adverse-effect severity, medication beliefs, social support, regimen complexity, and healthcare access remains possible.

5. Conclusion

Medication adherence among patients with breast cancer receiving oral systemic anticancer therapy was independently associated with overall health-related quality of life. Higher adherence was characterised by better functioning and lower symptom burden, whereas the associations of disease duration, treatment intent, and alcohol use with adherence were attenuated after adjustment. Concurrent assessment of medication adherence and quality of life may help identify patients who require more detailed evaluation and supportive care during long-term oral treatment. Longitudinal studies are needed to clarify the direction of this association and determine whether interventions targeting symptom burden and functional impairment can improve adherence.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Alanya Education and Research Hospital Ethics Committee (approval date: 10 December 2025; approval number: 18 – 12). Written informed consent was obtained from all participants before enrollment.

Consent to Participate

Written informed consent was obtained from all participants before their inclusion in the study.

Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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Author Contribution

G.K.S.: Conceptualization, Methodology, Investigation, Software, Writing—Original Draft, Project Administration, Data Curation, Visualization, and Formal Analysis. İ.B.: Investigation, Data Curation, Review and Editing and Supervision. O.Y.B.: Investigation and Data Curation. T.E.: Data Curation. M.S.: Data Curation. All authors reviewed and approved the final version of the manuscript.

Data Availability

The data supporting the findings of this study are not publicly available because of privacy and ethical restrictions related to patient confidentiality. De-identified data may be made available by the corresponding author upon reasonable request and subject to approval by the relevant ethics committee and applicable institutional regulations.

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