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ORIGINAL ARTICLE

A High Anticholinergic Burden Is Independently Associated With Nocturia in Turkish Older Women

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ABSTRACT

Objective: This study aimed to examine the relationship between nocturia and anticholinergic burden.

Methods: The female participants aged ≥65 years who presented to the outpatient geriatric clinic between November 2022 and January 2025 were retrospectively reviewed. Nocturia was defined as waking up from bed at night for urination at least twice per night. All participants underwent a comprehensive geriatric assessment (CGA). Demographic characteristics, comorbidities, geriatric syndromes, laboratory findings, and CGA parameters were recorded.

Results: Of 422 total patients, nocturia was present in 65.9% of them. Patients with nocturia were older ($p = 0.021$) and had higher rates of coronary artery disease ($p = 0.036$) heart failure ($p = 0.002$), and chronic lung disease ($p = 0.046$). Recurrent falls ($p = 0.005$), polypharmacy ($p < 0.001$), depression ($p < 0.001$), and lower gait-balance ($p = 0.033$) and activities of daily living scores ($p < 0.001$) were more frequent in the nocturia group. The proportion of patients with a high anticholinergic burden (Anticholinergic Cognitive Burden [ACB] score ≥3) was significantly higher in those with nocturia ($p = 0.024$). There was a significant association between high ACB scores and nocturia, independent of age (OR = 1.69; 95% CI: 1.05–2.69; $p = 0.028$), comorbidities (OR = 1.60; 95% CI: 1.01–2.60; $p = 0.048$), and laboratory parameters (OR = 1.63; 95% CI: 1.01–2.60; $p = 0.046$).

Conclusions: Our findings suggest that a higher anticholinergic burden is independently associated with nocturia in older female adults. Clinicians should be alert to anticholinergic burden as a modifiable factor in the management of nocturia in older female patients and consider deprescribing when appropriate.

1 | Introduction

Nocturia is a distressing and disruptive symptom of the lower urinary tract, particularly among older adults [1]. It is defined as waking from sleep one or more times to void; however, many studies consider two or more nightly episodes to be clinically significant [1, 2]. Although nocturia can occur at any age, its prevalence increases substantially with age [3]. It is reported to affect approximately 50% of individuals over the age of 60 years and nearly 80% of those over 80 years [4]. Thus, older age is considered the primary risk factor for nocturia [4].

Nocturia not only impairs quality of life but is also associated with several comorbidities, including diabetes mellitus, cardiovascular disease, chronic pulmonary conditions, neurological disorders, and increased mortality [5]. It contributes to poor sleep quality, an increased risk of falls, and the development of depressive symptoms [6]. Aging is accompanied by various changes in the urinary system, such as reduced bladder capacity, impaired urine concentration ability, and increased post-void residual volume [7]. In addition, age-related alterations in detrusor muscle function may lead to overactive bladder, a condition closely linked to nocturia [2]. Two major

physiological contributors to nocturia in older adults include altered vasopressin secretion and the nocturnal redistribution of body fluids from the lower extremities to the third space during recumbency [4].

The anticholinergic drug burden (ADB) is another important clinical concern frequently observed in older adults. It is associated with numerous adverse outcomes, including dry mouth, urinary retention, constipation, increased vulnerability to acute mental status changes, and cognitive decline [8]. Polypharmacy and the cumulative effects of drugs and their metabolites contribute significantly to the ADB [7]. In particular, the concurrent use of multiple medications with anticholinergic properties increases the risk of these undesirable effects in older adults [9]. Although antimuscarinic drugs constitute a subset of anticholinergic agents primarily used in the management of urinary symptoms, anticholinergic burden encompasses a broader range of medications across multiple therapeutic classes. Several rating tools have been developed to quantify anticholinergic activity in clinical practice, among which the Anticholinergic Cognitive Burden (ACB) scale is one of the most widely used and validated [10]. This scale assigns scores to medications based on their anticholinergic properties [11], with higher scores indicating a greater anticholinergic burden and an increased risk of adverse clinical outcomes. The ACB scale has been extensively applied in both clinical and observational studies involving older adults. Higher ACB scores have been associated with increased risk of falls and fall-related injuries in hospitalized older patients [12, 13]. Additionally, the ACB score has been identified as a significant predictor of in-hospital mortality among older adults [14].

The association between the ADB and various geriatric syndromes has been documented in numerous studies. The ADB has been linked to negative outcomes such as delirium, falls, prolonged hospital stays, and sarcopenia in older adults [15–18]. However, the relationship between the ADB and nocturia remains poorly explored in the existing literature. In this study, we aimed to investigate the relationship between nocturia and the ADB in older female adults. Existing studies have largely focused on nocturia secondary to urological conditions such as overactive bladder, and only a few have addressed nocturia as an independent outcome. This study aims to fill this gap by investigating the association between anticholinergic burden and nocturia, independent of known urological diseases. We hypothesize that a higher anticholinergic burden, as measured by the ACB scale, is associated with the presence of nocturia in older women.

2 | Materials and Methods

2.1 | Study Design

This retrospective, cross-sectional, and observational study involved the analysis of female patients over 65 years of age who applied to our outpatient geriatric clinic between November 2022 and January 2025. A total of 422 female patients were included in the study. The participant selection process is summarized in Figure 1.

Each patient underwent a comprehensive geriatric assessment (CGA).

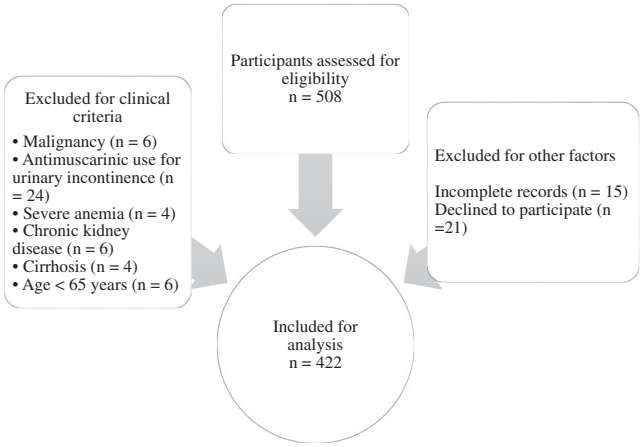

FIGURE 1 | Diagram of participant selection and inclusion process.

2.2 | Inclusion Criteria

Female patients over the age of 65 years who applied to our centre for any reason and did not meet any of the exclusion criteria were included in the study.

2.3 | Exclusion Criteria

The study exclusion criteria were:

- Presence of active malignancy;
- Severe anemia (hemoglobin < 7 g/dL);
- Cardiac events such as acute heart failure, acute coronary syndrome, and severe aortic stenosis;
- Advanced chronic renal disease (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2);
- Patients receiving antimuscarinic medications for the treatment of urinary incontinence;
- Decompensated liver cirrhosis;
- Sepsis;
- Acute rheumatic or inflammatory diseases;
- Alcohol and/or substance addiction;
- A history of an acute cerebrovascular accident;
- Patients with immobility;
- Patients with acute urinary tract infections;
- Male patients;
- A Clinical Dementia Rating > 2.

Patients receiving antimuscarinic medications for the treatment of urinary incontinence were excluded to minimize direct pharmacological confounding. Other medications with anticholinergic effects were included and evaluated using the ACB scale.

Although antimuscarinic therapy was excluded, urinary incontinence subtypes—particularly functional urinary incontinence—were not systematically classified, and therefore

residual confounding related to functional impairment cannot be completely excluded.

2.4 | Patient Characteristics

Demographic data (age, education level, and marital status) and comorbidities (hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, cerebrovascular disease, peripheral vascular disease, osteoporosis, atrial fibrillation, and chronic lung disease) were recorded.

All medications that the patients were regularly using at the time of their first outpatient clinic visit were recorded during the comprehensive geriatric assessment, and ACB scores were calculated accordingly.

Laboratory parameters including glucose, hemoglobin, creatinine, uric acid, the eGFR, albumin, sodium, potassium, calcium, phosphate, ferritin, magnesium, vitamin D, vitamin B12, folic acid, and blood urea nitrogen (BUN) were evaluated. Geriatric syndromes—including probable sarcopenia, a history of falls, malnutrition, depression, frailty, and orthostatic hypotension—were assessed by an experienced geriatrician.

2.5 | Comprehensive Geriatric Assessment Parameters

All participants underwent the following tests as part of a CGA:

- Yesavage Geriatric Depression Scale (YGDS);
- Tinetti Performance Oriented Mobility Assessment (POMA);
- Barthel Activities of Daily Living Index (ADL);
- Lawton-Brody Instrumental Activities of Daily Living (IADL);
- Mini Nutritional Assessment—Short Form (MNA-SF) [19].

2.6 | Nocturia Definition

Nocturia is defined as waking up one or more times to urinate, interrupting sleep at night. Clinical studies have shown that urinating ≥ 2 times has significant effects on quality of life and is therefore considered to be the threshold for clinically significant nocturia [20]. The nocturia status was determined by asking each participant how many times they had to get out of bed at night to urinate in the last 30 days.

2.7 | Assessment of the ADB

The ADB of the medications used by the patients was assessed based on the ACB scale. The score is interpreted as follows:

- ACB = 0 indicates no anticholinergic effect;
- ACB = 1 indicates a possible anticholinergic load;
- ACB = 2–3 indicates a definite anticholinergic load [21].

Antimuscarinic agents used specifically for urinary incontinence were excluded to reduce potential confounding, as they may directly alter nocturia symptoms regardless of overall anticholinergic exposure.

2.8 | Statistical Analysis

The participants were divided into two groups according to their nocturia status. Categorical variables are presented as percentage (%), and continuous variables are presented as the mean ± standard deviation. Categorical variables were compared between the two groups using the chi-square test. The Kolmogorov–Smirnov test was used to determine whether the continuous variables followed a normal distribution. Because they did not, they were compared using the Mann–Whitney U test. The relationship between the nocturia status and the ACB score was assessed with binomial regression, adjusting for confounding factors. Accordingly, the odds ratio (OR) with a 95% confidence interval (CI) was calculated for model 0 (unadjusted), model 1 (age-adjusted), model 2 (model 1 adjusted for comorbidities), and model 3 (model 2 adjusted for laboratory findings). A p value < 0.05 was considered to indicate a statistically significant difference. All statistical analyses were conducted using SPSS Statistics version 22.0 (IBM Corp, Armonk, NY).

2.9 | Ethical Issues

The study was approved by the Balikesir University Health Sciences Non-Interventional Research Ethics Committee (Approval No: 2025/177; Date: 06/05/2025) and conducted in accordance with the Declaration of Helsinki.

3 | Results

A total of 422 female geriatric patients were included in the study; 278 (65.9%) of them had nocturia, and 144 (34.1%) did not have nocturia. The patients with nocturia were significantly older than the patients without nocturia (78.45 ± 5.79 vs. 77.12 ± 7.1 years; $p = 0.021$). Table 1 summarizes the demographic characteristics, comorbidities, and laboratory findings of the patients. The frequency of coronary artery disease, congestive heart failure, and chronic lung disease was significantly higher in the nocturia group ($p < 0.05$). The laboratory findings were similar between the two groups ($p > 0.05$).

The number of recurrent falls and medications used was significantly higher in the nocturia group compared with the non-nocturia group ($p < 0.05$). The frequency of geriatric depression was higher in the nocturia group ($p < 0.05$). The gait-balance and basic ADL scores were significantly lower in the nocturia group ($p < 0.05$) (Table 2). The percentage of patients with an ACB score ≥ 3 was significantly higher in the nocturia group (32.7%) compared with the non-nocturia group (22.2%) ($p < 0.05$) (Figure 2).

We performed binary logistic regression to evaluate the relationship between the anticholinergic burden, based on the

TABLE 1 | Comparison of demographic characteristics, comorbid diseases, and laboratory findings according to nocturia status.

	Nocturia (+)	Nocturia (−)	
	***n* = 278**	***n* = 144**	***p***
Demographic features			
Age (mean ± SD)	78.45 ± 5.79	77.12 ± 7.1	0.021*
Education year (mean ± SD)	3.38 ± 2.34	3.12 ± 2.29	0.574
Marital status (married %)	39.2	47.2	0.238
Number of child (mean ± SD)	2.76 ± 1.27	2.93 ± 1.76	0.420
Comorbidities (%)			
Hypertension	80.6	73.6	0.100
Diabetes mellitus	41.4	39.6	0.724
Coronary artery disease	21.6	13.2	0.036*
Congestive heart failure	15.1	4.9	0.002*
Peripheral arterial disease	4.7	6.3	0.490
Osteoporosis	34.5	30.6	0.411
Atrial fibrillation	16.5	9.7	0.057
Chronic lung disease	21.9	13.9	0.046*
Cerebrovascular disease	2.2	4.2	0.239
History of hysterectomy	8.6	7.6	0.480
Laboratory findings (mean ± SD)			
Glucose (mg/dL)	133.5 ± 68.5	136.6 ± 53.2	0.889
Hemoglobin (g/dL)	12.28 ± 1.19	12.5 ± 1.54	0.069
Blood urea nitrogen (mg/dL)	19.39 ± 6.52	17.19 ± 4.45	0.918
Creatinine (mg/dL)	0.94 ± 0.36	0.83 ± 0.19	0.069
Uric acid (mg/dL)	5.36 ± 1.98	5.2 ± 1.44	0.299
eGFR (mL/min)	63.4 ± 19.81	70.13 ± 16.66	0.056
Albumin (gr/dL)	4.11 ± 0.25	4.08 ± 0.32	0.651
Sodium (mmol/L)	138 ± 2.78	138.8 ± 2.21	0.079
Potassium (mEq/L)	4.37 ± 0.43	4.33 ± 0.30	0.512
Calcium (mg/dL)	9.5 ± 0.47	9.34 ± 0.53	0.921
Phosphate (mg/dL)	3.48 ± 0.52	3.37 ± 0.59	0.276
Ferritin (ng/mL)	43.8 ± 55.07	44.78 ± 57.76	0.796
Magnesium (mg/dL)	1.85 ± 0.21	1.92 ± 0.22	0.378
25-hydroxy Vitamin D (μg/L)	22.3 ± 14.72	17.61 ± 12.49	0.867
Vitamin B12 (ng/L)	388.08 ± 299.31	337.44 ± 246.26	0.199
Serum folate	9.76 ± 4.54	8.36 ± 2.81	0.642

Abbreviation: SD, Standard deviation.
*$p < 0.05$ was considered statistically significant.

ACB score, and the nocturia status. We observed a significant association between a high anticholinergic burden and the presence of nocturia (Table 3). In the unadjusted model (model 0), a higher ACB score increased the risk of nocturia (OR = 1.70; 95% CI: 1.06–2.71; $p = 0.025$). This association remained significant after adjusting for age (model 1: OR = 1.69; 95% CI: 1.05–2.69; $p = 0.028$); age and comorbidities (hypertension, coronary artery disease, congestive heart failure, and

TABLE 2 | Comparison of geriatric syndromes and comprehensive geriatric assessment parameters according to nocturia status.

	Nocturia Yes $n=278$	Nocturia No $n=144$	p
Geriatric syndromes			
Probable sarcopenia (%)	45.5	38.5	0.171
Number of falls in a year (mean ± SD)	2.38 ± 3.62	1.04 ± 1.64	0.005*
Malnutrition (%)	35.3	33.3	0.694
Number of medications (mean ± SD)	7.66 ± 3.71	4.36 ± 2.32	< 0.001*
Geriatric depression (%)	61.9	45.1	< 0.001*
Frailty (%)	44.2	37.5	0.183
Orthostatic hypotension (%)	40.5	35.5	0.334
POMA	21.35 ± 5.33	21.64 ± 5.85	0.033*
TUG duration (sec)	23.76 ± 12.84	21.12 ± 12.03	0.011*
YGDS	5.92 ± 3.65	5.41 ± 3.51	0.033*
Basic ADLs	82.12 ± 11.92	85.8 ± 14.62	< 0.001*
Instrumental ADLs	15.43 ± 5.1	15.12 ± 5.03	0.809

Abbreviations: ADLs, activities of daily living; POMA, performance-oriented mobility assessment; TUG, timed up and go; YGDS, Yesavage geriatric depression scale.
*$p < 0.05$ was considered statistically significant.

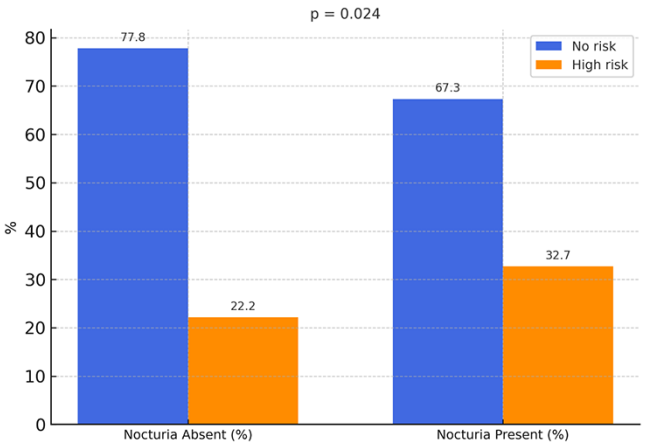

FIGURE 2 | Relationship between nocturia status and anticholinergic burden score. Patients with nocturia had a higher anticholinergic burden (ACB score ≥ 3) compared with those without nocturia.

TABLE 3 | Relationship between anticholinergic load and nocturia status by Logistic regression analysis.

	Odds ratio	95% confidence interval	p
Model 0	1.70	1.06–2.71	0.025*
Model 1	1.69	1.05–2.69	0.028*
Model 2	1.60	1.01–2.60	0.048*
Model 3	1.63	1.01–2.60	0.046*

Note: Model 0—Unadjusted model, Model 1—Age-adjusted model, Model 2—Model 1 plus adjusted for Hypertension, Coronary Artery Disease, Congestive Heart Failure, Chronic lung disease, Model 3—Model 2 plus adjusted for the level of hemoglobin, eGFR, sodium.
*$p < 0.05$ was considered statistically significant.

chronic lung disease) (model 2: OR = 1.60; 95% CI: 1.01–2.60; $p = 0.048$); and age, comorbidities, and laboratory parameters (model 3: OR = 1.63; 95% CI: 1.01–2.60; $p = 0.046$).

4 | Discussion

We demonstrated a possible association between a high anticholinergic burden and the risk of nocturia in older female adults. This association occurred independently of potential confounding factors.

While the International Continence Society defines nocturia as getting up from bed more than once at night to urinate, urinating twice or more is associated with adverse outcomes [22, 23]. The frequency of nocturia increases with age. Although there is no reported gender difference, in clinical practice, nocturia is thought to be more common in men due to prostate disorder, including benign prostatic hypertrophy. Nevertheless, women experience nocturia as frequently as men [23]. Nocturia has been reported in more than 50% of people over the age of 60 years, and in up to 80% in individuals over the age of 80 years [4]. In another study, the prevalence of nocturia among women over 60 years living in the United States with ≥ 1 and ≥ 2 nocturia episodes was approximately 85% and 50%, respectively [24]. The prevalence of nocturia in older adults in Türkiye is unknown. In our study, the frequency of nocturia in women over 65 years of age was 65.9%.

Nocturia is a condition that negatively affects the quality of life for older adults. In addition, it is associated with serious clinical outcomes such as falls, fractures, sleep disorders, depression, cognitive impairment, and increased mortality [5, 25, 26]. Two or more episodes of nocturia in elderly women are also an indicator of a poor health status [2]. Therefore, there is a significant increase in health expenditures for older adults experiencing nocturia. Consistent with the literature, we found that the nocturia group presented a higher frequency of depression, more falls in the last year, a higher number of medications used, and lower balance and walking test and basic ADL scores compared with the group without nocturia. Recent evidence demonstrates that functional urinary incontinence in older women is strongly associated with impaired activities of daily living, reduced gait and balance performance, decreased muscle strength, malnutrition,

and depressive symptoms. In line with these findings, patients with nocturia in our cohort exhibited higher rates of falls, functional dependency, and depressive symptoms, suggesting that nocturia may reflect underlying functional vulnerability in a subset of older women rather than an isolated urological condition [27]. There are conflicting published data regarding the direct relationship between frailty and nocturia among geriatric syndromes; only a few studies have demonstrated a relationship between the two conditions [28]. We did not observe a difference in frailty between individuals with and without nocturia. When considering the causes of nocturia in women, age stands out as one of the most important factors [29]. While nocturia is generally considered to be a consequence of chronic diseases, it should be considered a disorder that primarily affects older people [29]. Although nocturia can develop in older women with an overactive bladder, it can also occur in women without any urinary problems. In addition, a history of hysterectomy, being postmenopausal, and the parity status can also be considered causes of nocturia. However, a comprehensive evaluation for nocturia in older women, independently of urogynaecological history, is necessary [29]. Questioning medication use in older adults is a particularly important aspect regarding the assessment of nocturia.

Polypharmacy is well known to be associated with adverse outcomes in older adults. While polypharmacy in older adults can improve underlying health conditions, it can also lead to numerous adverse outcomes [30], especially regarding the use of anticholinergic medications. These medications are used in the treatment of conditions such as Parkinson's disease, depression, insomnia, asthma, allergic conditions, chronic obstructive pulmonary disease, and overactive bladder [31, 32], and their use increases with age. Anticholinergic medication use can lead to cognitive impairment, falls, fall-related fractures, delirium, and deterioration in quality of life and activities of daily living in older adults [33, 34]. It is important to assess the ADB, a subcategory of polypharmacy, in geriatric practice. There are numerous methods to measure the ADB, although there is not a consensus on which one is the best. Among these, the ACB scale is a frequently used and useful method across a broad range of medications [35, 36]. Additionally, researchers have examined the relationship between the ADB and conditions important in geriatric practice, such as malnutrition and oropharyngeal dysphagia [37, 38]. However, there has been no study regarding the relationship between nocturia and the ADB. We have demonstrated this relationship, and it is independent of confounding factors.

A comprehensive examination of the relationship between nocturia and the anticholinergic burden revealed that urinary system complaints such as nocturia are common in patients receiving anticholinergic medications for conditions such as dementia. Furthermore, nocturia is also prevalent in patients with conditions such as Parkinson's disease and atypical parkinsonism, where autonomic dysfunction is prominent. Nocturia can be observed in 90% of patients diagnosed with multiple system atrophy. In addition, there are three possible mechanisms that could explain the relationship between nocturia and a high ADB. First, a high ADB contributes significantly to urinary retention and reduced detrusor contractility, which can worsen nocturnal bladder storage abnormalities [39]. Second, diminished renal concentrating ability and disrupted circadian patterns of vasopressin secretion predispose a person to nocturia, and a high ADB may exacerbate nocturnal polyuria in older adults [40]. Third, central anticholinergic effects such as sleep fragmentation increase nocturnal arousals, increasing awareness of bladder fullness and prompting voiding [39]. Clinicians are encouraged to consider the ADB when evaluating unexplained nocturia in older patients. Proactive deprescribing strategies may help mitigate the impact of a high ADB on nocturia and enhance overall quality of life. Prospective or interventional studies are needed to better elucidate the causal relationship between anticholinergic burden and nocturia and to evaluate its impact on clinical outcomes.

The strength of our study is that it is the first to demonstrate an association between nocturia and a high ADB based on the ACB score, and this association was independent of confounding factors. Patients receiving antimuscarinic medications for the treatment of urinary incontinence were deliberately excluded from the study in order to eliminate the potential confounding effects of these agents on nocturia. Nevertheless, our study has several limitations. First, our study is retrospective and cross-sectional, which limited our ability to determine causality. Second, we did not demonstrate whether the relationship between nocturia and the anticholinergic burden is related to specific anticholinergic drug groups (e.g., antidepressants, antipsychotics, or antihistamines). Therefore, it remains unclear whether certain drug classes contribute more significantly to nocturia risk. Third, although patients using antimuscarinic medications were excluded to minimize direct pharmacological confounding, this may limit the generalizability of our findings to real-world geriatric populations, in which such medications are frequently prescribed.

5 | Conclusions and Implications

We showed that the anticholinergic burden may be associated with nocturia in women aged 65 years and older. In clinical practice, the anticholinergic burden should be considered when prescribing drugs, especially in older adults, and alternative drug options should be evaluated when necessary. In addition, in the presence of nocturia, not only the urinary system but also the general geriatric condition should be considered in detail.

Author Contributions

Concept: Y.O., S.E.K. Design: Y.O., S.E.K. Supervision: S.E.K. Resources: Y.O., S.E.K. Materials: Y.O., S.E.K. Data Collection and/or Processing: Y.O., S.E.K. Analysis and/or Interpretation: S.E.K. Literature Search: Y.O., S.E.K. Writing Manuscript: Y.O. Critical Review: S.E.K.

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The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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