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Complementary advantages of microsurgical treatment for vertebral artery dolicoarteriopathies: Mitigating symptoms of restless leg syndrome in refractory vertebrobasilar insufficiency

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ABSTRACT

Objective: This retrospective study examines the impact of microsurgical treatment on vertebral artery (VA) dolicoarteriopathies and associated restless leg syndrome (RLS) in patients with refractory vertebrobasilar insufficiency (VBI).

Patients and Methods: We analyzed 78 patients with grade 2 and 3 kinks, and found out that the targeted microsurgical interventions, primarily designed to address VBI, improved secondary RLS symptoms in 12 patients. Procedures included arteriolysis and, depending on severity, grafting. Statistical analysis was conducted using Stata 16 (StataCorp LP, Texas, USA).

Results: In twelve patients aged 55 to 72 years with refractory VBI and drug-resistant RLS, micro-neurosurgical correction of V1 segment dolicoarteriopathy, abnormal elongation and kinks in the artery, demonstrated promising outcomes. Postoperatively, 83.33% (10 patients) reported complete resolution of RLS symptoms, and 16.66% (2 patients) experienced partial symptom relief ($p<0.05$). Overall, 86.8% of various VBI-related symptoms were significantly improved or resolved ($p<0.05$). The microsurgical technique, avoiding traditional flow-arresting procedures, proved to be highly effective in this preliminary study with no mortality and minimal temporary complications, underscoring its potential treatment avenue for such complex neurovascular conditions.

Conclusion: This study illuminates the relationship between VBI and RLS, proposing a potential vascular etiology for RLS, and highlights the need for a broader diagnostic approach for patients with refractory VBI.

Keywords: Vertebral artery dolicoarteriopathy, Microsurgical treatment, Restless leg syndrome, Vertebrobasilar insufficiency

1. INTRODUCTION

Vertebral artery (VA) dolicoarteriopathy, characterized by the pathological elongation, kinking, or coiling of the VA, has been increasingly recognized as a contributing factor to a spectrum of cerebrovascular pathologies [1,2]. Kinks are classified according to Metz et al., classification according to the severity of the angle [3]. (Grade 1:90-60 degrees (mild kinging), Grade 2: 60-30 (moderate kinging), Grade 3 < 30 degrees (severe kinging)). Especially, in grade 2 and 3 dolichoarteriopathies, there is a reduction in blood flow, which escalates the risk of ischemic events [4]. In simpler terms, a 'dolicoarteriopathy' is when a VA is abnormally long and twisted, which can sometimes squeeze or restrict blood flow to the brain, increasing the risk of stroke-like episodes and even imitating Parkinsonism-like symptoms [5]. These vascular aberrations can disrupt hemodynamic stability and play a role in vertebrobasilar insufficiency (VBI) pathophysiology, manifesting in a clinical spectrum that includes symptoms from cervicogenic dizziness to radiculopathy [6,7]. In cases of refractory VBI, when endovascular surgery is not feasible or appropriate, primary surgical interventions such as classical techniques, including bypass techniques, and new microsurgical interventions may be performed. These surgical procedures address the specific vascular anomalies in VBI, offering alternative avenues for restoring cerebral hemodynamics and alleviating the associated neurological symptoms [8-10].

Restless legs syndrome (RLS) or Willis–Ekbom disease is a prevalent sensorimotor disorder characterized by an irresistible urge to move the legs, especially during sleep or periods of inactivity, dramatically affecting the patients' quality of life [11]. Although, the etiology of RLS remains multifaceted, growing evidence suggests its connection with vascular pathologies

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extending from the cerebrovascular to cardiovascular domains [12]. Given the widespread occurrence of RLS, understanding its vascular implications is paramount, especially when considering ischemic conditions [13,14]. A recent research has particularly highlighted ischemic alterations in the brainstem, left amygdala, and globus pallidus, implicating these limbic, medial frontal region, and basal ganglia structures as critical components in the neurophysiological pathways of RLS [15]. Previous studies have underscored the association of RLS with an elevated risk of hypertension, heart disorders, iron deficiency, kidney diseases, and stroke [16,17]. Moreover, cerebral small vessel disease (SVD) has been implicated in RLS, with studies highlighting the prevalence of silent cerebral SVD in RLS patients without a history of stroke [18]. However, although these vascular correlations provide valuable insights, a gap exists in our understanding of etiology and potential therapeutic interventions that address the underlying vascular pathologies when we analyzed VA dolicoarteriopathy-related refractory VBI.

Clinical observations suggest a possible vascular etiology, particularly implicating anatomical abnormalities of the VA, such as dolicoarteriopathies, leading to VBI and RLS. This understanding is particularly crucial when considering VBI, which can affect brain regions critical for RLS [19]. Our retrospective study targets a specific patient group with medically resistant RLS co-occurrence with refractory VBI due to VA dolicoarteriopathies, which are deemed by endovascular interventionalists as unsuitable cases. Novel micro-neurosurgical approaches to the V1 segment of the VA, primarily to address VBI, also inadvertently resulted in the resolution of RLS symptoms. This unanticipated observation has prompted a more rigorous retrospective examination to elucidate the potential etiopathogenic relationship and therapeutic implications between these clinical manifestations and refractory VBI. Therefore, we aimed to evaluate the effect of microsurgical treatment on V1 segment dolicoarteriopathies and its concomitant impact on RLS in patients with refractory VBI.

2. PATIENTS and METHODS

Patient population and selection criteria

We retrospectively analyzed 78 patients who underwent surgical procedures primarily for refractory VBI due to dolicoarteriopathy (grade 2 and 3 kinks) of the V1 segment from 2016 to 2023. All surgeries were performed by the senior surgeon, with informed consent obtained from all participants. The local ethics committee approved the study, documented under approval number 2/12 dated 03.30.2022.

Patients included in this study were initially diagnosed with RLS at external centers utilizing a standardized questionnaire aligned with the 2003 International RLS Study Group criteria [20], subsequently verified by a neurologist. These individuals also presented with VBI symptoms and were undergoing medical management; however, they continued to experience persistent, life-impacting symptoms despite these maximum therapeutic interventions. Each patient underwent a thorough diagnostic process, including brain magnetic resonance imaging (MRI) and brain and cervical MR angiography starting from the aortic arch. Brain MRI is employed primarily to rule out additional intracranial pathologies, and MR angiography assesses the integrity of collateral circulation. Cervical MR angiography shows the lesion or anomaly in two VAs or one VA with hypofunction in the other VA that supports the diagnosis beside the clinic. Follow-up assessments were conducted within 3-6 months of recruitment. They had an average follow-up period of one year.

We meticulously recorded symptoms indicative of VBI, such as drop attacks, dysarthria, diplopia, dysphagia, dizziness, visual field defects, hemihypoesthesia, hemiparesis, ataxia, and dysmetria. To maintain the integrity of the study and ensure a clear association between the vascular pathologies and the symptoms observed, we implemented strict exclusion criteria. We excluded patients with endovascular candidates, medically responsive patients, and neurological disorders, including neuropathies or central nervous system conditions that could independently cause symptoms similar to RLS. This rigorous screening was vital to isolate the impact of refractory VBI and related vascular dolicoarteriopathy on the manifestation of medically resistant RLS symptoms in the patient group. The comparative analysis evaluated the preoperative conditions and postoperative surgical effectiveness for patients with the coexistence of RLS alongside VBI.

Surgical technique

After exposing the V1 segment of the VA, arteriolysis (removal or dissection of fibrous bands surrounding the artery to alleviate the stenosis and restore blood flowMetin girmek için buraya tıklayın veya dokunun.) was performed [21-23]. For significant kinks (grades 2 and 3) in the V1 segment, treatment varied with kink severity. Arteriolysis alone or with the traction of the subclavian artery (SCA) addressed moderate elongation, such as grade 2 kinks, as shown in Figure 1. In contrast, the severe elongation of the vessel involved grafting to reposition the VA, such as for grade 3 kinks, as demonstrated in Figure 2. Surgical precision was paramount to preserve vascular integrity.

Statistical analysis

Data analysis was conducted using Stata 16 (StataCorp LP, Texas, USA). Descriptive statistics were employed to summarize patient characteristics, preoperative symptoms, and postoperative 6. month follow-up symptom evaluation. The frequency and percentage of patients experiencing complete resolution or partial improvement of RLS symptoms following micro-neurosurgical intervention were calculated. A paired t-test was used to compare preoperative symptom severity and postoperative improvement in patients with refractory VBI. Symptom based assesment was performed using McNemar's test for related samples due to the binary nature of the outcome (improvement: yes/no). A p-value of less than 0.05 was considered indicative of statistical significance.

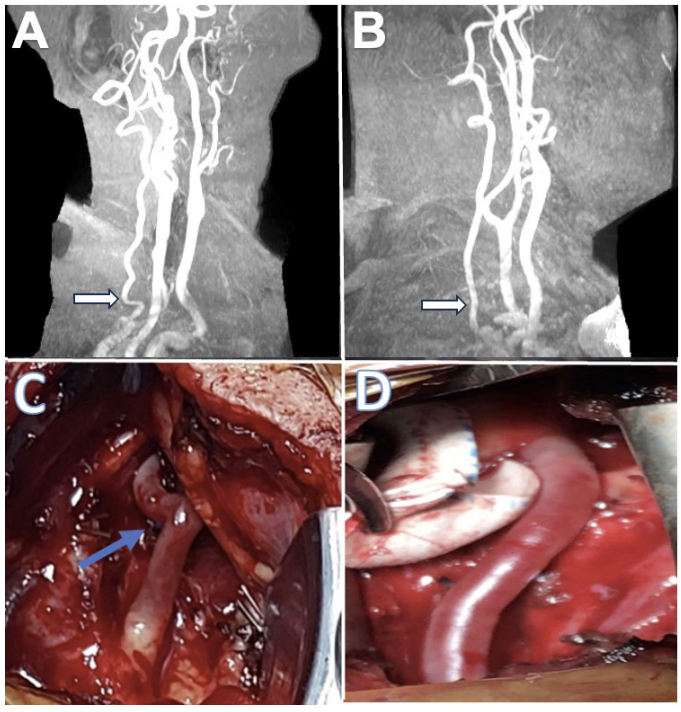

Figure 1. *A: Preoperative MR angiographic visualization of the grade 2 kink in the V1 segment (white arrow). B: Postoperative MR angiography image showing the vertebral artery after surgical correction of the grade 2 kink (white arrow). C: Perioperative microscopic image displaying the V1 segment of VA with grade 2 kinking (blue arrow) D: Perioperative microscopic view after the surgical correction.*

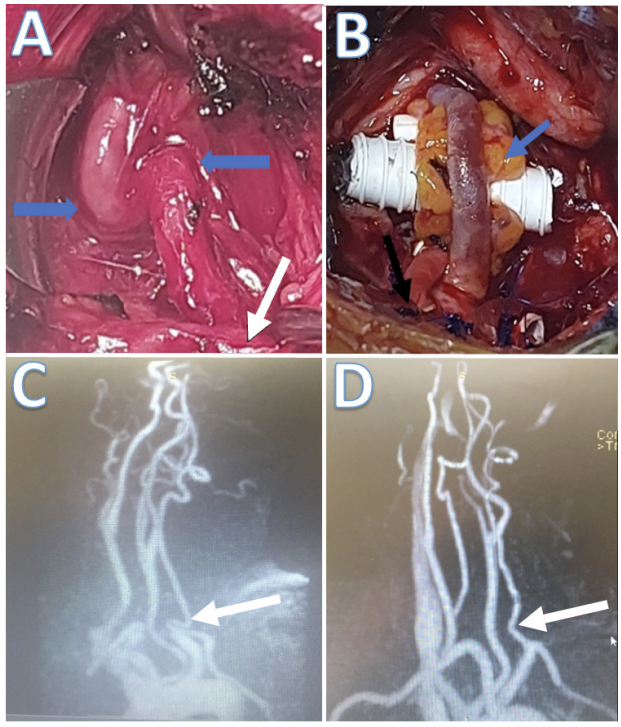

Figure 2. *A: Perioperative microscopic visualization of the grade 3 kink in the V1 segment (blue arrows) and subclavian artery (white arrow). B: Perioperative microscopic view after the surgical correction of grade 3 kink using vessel and adipose tissue grafts (blue arrow). C: Preoperative MR angiography image displaying the V1 segment of VA with grade 3 kinking (white arrow) D: Postoperative MR angiography image after the surgical correction (white arrow).*

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Table I. *Clinical outcomes of micro-neurosurgical intervention in RLS for vertebral artery (V1 segment) dolicoarteriopathies*

Condition	Total Patients	Complete Resolution	Partial Improvement
Restless Leg Syndrome	12	10 (83.33%)	2 (16.66%)

Table II. *Preoperative symptoms and postoperative improvement rates of the refractory vertebrobasilar insufficiency symptoms*

Patient No.	Preoperative Symptoms	Postoperative Improvement
1	Dysmetria,Intentional Tremor,Ataxia,Dysphagia	Completely Resolved
2	Dysmetria,Intentional Tremor,Dizziness,Hemihipoestesia	Markedly Improved
3	Dysmetria,Intentional Tremor,Ataxia,Drop Attacks	Completely Resolved
4	Dysmetria,Intentional Tremor,Dizziness,Ataxia	Completely Resolved
5	Dysmetria,Intentional Tremor,Ataxia,Diplopia	Completely Resolved
6	Dysmetria,Intentional,Tremor,Dizziness,Ataxia, Drop Attacks	Completely Resolved
7	Dysmetria,Intentional Tremor,Dysphagia,Dysartria	Markedly Improved
8	Dysmetria,Intentional Tremor,Dizziness,Visual Field Defects	Completely Resolved
9	Dysmetria,IntentionalTremor,Ataxia,Dizziness,Diplopia	Completely Resolved
10	Dysmetria,Intentional Tremor,Dizziness,Ataxia	Completely Resolved
11	Dysmetria,Intentional Tremor,Dizziness,Ataxia	Completely Resolved
12	Dysmetria,Intentional Tremor,Dizziness,Ataxia	Completely Resolved

3. RESULTS

Our retrospective study evaluated the impact of micro-neurosurgical interventions on patients suffering primarily from refractor VBI due to V1 segment dolicoarteriopathy and its effect secondarily for medically resistant RLS symptoms. The patient cohort consisted of 12 individuals aged 55 to 72 years, with a mean age of 63. The group included a mixture of grade 2 and Grade 3 kinks (4 grade 2 kinks,8 grade 3 kinks) according to the Metz criteria in the V1 segment, indicative of varying degrees of severity in their condition. Following microsurgery, all the arterial kinks were rectified using new techniques that obviated the need for traditional flow-arresting procedures such as bypass.

Following the surgical procedures, a notable improvement in RLS symptoms was observed across the cohort. Specifically, 10 patients (83.33%) experienced complete resolution of RLS symptoms, evidencing the intervention's potential in treating the neurological manifestations associated with V1 segment dolicoarteriopathy. However, 2 patients (16.66%) showed partial improvement, indicating a reduction but not a complete cessation of symptoms ($p<0.05$), as shown in Table I.

Our study focused on 12 patients with refractory VBI, who presented with a spectrum of debilitating symptoms, including intentional tremors, drop attacks, dysarthria, diplopia, dysphagia, dizziness, visual field defects, hemihypoesthesia, ataxia, and dysmetria. Significant clinical improvement was observed following micro-neurosurgical interventions tailored to address VA dolicoarteriopathy, as demonstrated in Table II. The paired t-test revealed a significant reduction in symptom severity postoperatively ($p < 0.05$ for all compared symptoms). Table II summarizes the clinical outcomes of the patients' post-micro-neurosurgical intervention for refractory VBI, highlighting the overall success rate.

In assessing the overall symptomatic improvement postoperatively, our data indicates that approximately 86.8% of the observed symptoms across all patients were resolved entirely or markedly improved. This outcome suggests a high efficacy rate for the surgical technique implemented in our study, reinforcing its potential as a valuable treatment modality for patients with VBI who are unresponsive to medication. No operative mortality and low temporary morbidities such as ptosis, swallowing difficulties, hoarseness, and coughing were encountered.

The results suggest that in light of the clinical presentations observed, our proposed approach primarily addresses patients presenting with refractory VBI who also exhibit medically resistant RLS. In such cases where medical therapy has proven ineffective, and the patient's condition persists, it becomes imperative to consider the presence of VA anomalies, specifically dolicoarteriopathies in the cervical region.

4. DISCUSSION

In this retrospective study, we uncovered that micro-neurosurgery for VA dolicoarteriopathy resulted in complete resolution of RLS symptoms in 83.33% (10 out of 12) patients and partial improvement in 16.66% (2 out of 12) patients, with an overall symptomatic improvement rate of 86.8% for various refractory VBI-related symptoms. These findings underscore the potential of microsurgery as a pivotal treatment for VBI-related symptoms and emphasize the vascular relation of RLS. The findings align with emerging studies suggesting a vascular component to this traditional neurological syndrome.

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The quantitative leap in symptom management observed postoperatively reinforces the argument for a vascular evaluation in RLS patients, especially those who do not respond to standard pharmacotherapy. Our data contributes to the evidence suggesting that micro-neurosurgical interventions may substantially improve the quality of life for these patients with complex neurovascular disorders, challenging the conventional pharmacological treatment alone.

Our retrospective analysis yielded a pivotal observation: patients undergoing micro-neurosurgical intervention for refractory VBI exhibited a notable resolution of RLS despite the absence of ischemic findings on MRI. This finding aligns with current literature, which often associates these symptoms with brain regions correlated with vertebrobasilar system feeding territory. The absence of overt ischemic changes on MRIs in our patients underscores the necessity of reevaluating the neurovascular interplay in RLS, advocating for a broader diagnostic lens encompassing structural and functional cerebral vascular integrity. When appropriate and feasible, endovascular therapy is often the first line of intervention. However, open surgical techniques, such as those employed in our patients, may be considered in scenarios where endovascular treatment is either ineffective or not feasible due to the surrounding fibrotic tissue and the significant angulation present, particularly in grade 2 and 3 kinks, which can compromise the success of endovascular interventions and may even pose additional risks. These new micro-neurosurgical methods offer an alternative for managing VA dolicoarteriopathies, potentially alleviating the complex symptoms associated with these vascular anomalies. Further research with larger sample sizes is warranted to confirm these findings and to refine surgical approaches for optimal patient outcomes.

The interrelation between RLS and vascular pathologies has become a focal point in recent neurological research. A series of studies have illuminated the prevalence of RLS following stroke, with an estimated occurrence in 10% of patients, underscoring the potential vulnerability of specific brain regions to ischemic events even though there are no MR image abnormalities [24,25]. The predictive quality of RLS for subcortical stroke has also been substantiated, with unilateral or asymmetrical RLS symptoms frequently preceding cerebrovascular incidents. This association advocates for a more vigilant approach to RLS as a possible early indicator of subcortical vascular complications. Moreover, the negative impact of RLS on post-stroke quality of life has been documented, raising the imperative for routine screening and potential treatment of RLS in the wake of cerebrovascular events to enhance patient recovery and well-being [26,27]. When RLS presents as an isolated condition, it is associated with various brain regions; however, when it precedes ischemic events and coexists with VBI, it suggests a more localized pathology. In such cases, the medial border zone, corresponding to the paracentral lobule where the anterior and posterior pericallosal arteries converge—essentially the interface between anterior and posterior circulation—may be the primary target area. This region, being part of the border zone territories, is known to be particularly vulnerable to ischemia, often being the first to be affected. This insight is crucial for the discussion section as it aligns the neurovascular implications of RLS with underlying ischemic conditions.

In light of the evidence in recent literature, RLS has been associated with alterations in several brain regions, including the anteromedial pons, body of the caudate nucleus, cingulate gyrus, medial frontal region, and paracentral lobule, limbic system, globus pallidus, and hippocampus [15,24,28]. These findings have elucidated a neural circuitry that could be vulnerable to vascular insufficiencies, especially in the vertebrobasilar feeding territory. In our current study, we observed that symptoms of RLS often presented in conjunction with symptoms indicative of VBI. Notably, these symptoms persisted despite resistance to medical therapy and the presence of dolicoarteriopathies, which were deemed unsuitable for endovascular treatment, thus necessitating surgical intervention.

The importance of a comprehensive vascular assessment, especially concerning the vertebrobasilar system, becomes apparent in patients presenting with RLS. Given the efficiency of current treatments, recognizing the vertebrobasilar system to RLS can significantly improve patient management. This approach may alleviate the refractory VBI and can benefit from the medically resistant RLS and address underlying vascular anomalies that could predispose individuals to more severe cerebrovascular events.

Our study's retrospective design and the limited number of participants may affect the breadth of our conclusions. The findings of our retrospective study should be considered in the context of its inherent limitations. Primarily, the relatively small sample size and the patients' specificity may limit our results' generalizability. Larger-scale, multicenter studies are necessary to corroborate our findings across diverse populations and clinical settings. Additionally, the observational nature of our study limits the ability to draw causal inferences between microsurgical interventions and improvement in RLS symptoms.

Furthermore, the average follow-up period of one year, while insightful, does not allow for the assessment of long-term outcomes and sustainability of symptom relief. Longer-term follow-up studies are essential to understand the durability of clinical improvements post-intervention.

Finally, while our study provides valuable insights into the clinical improvement of RLS symptoms following microsurgical intervention for VA dolicoarteriopathies, the underlying mechanisms remain fully elucidated. Establishing a clear mechanistic link between these interventions and improvements in RLS symptoms warrants further investigation. Future research should include more significant, prospective trials to confirm the efficacy of micro-neurosurgical interventions for refractory VBI and the secondary benefits of RLS. For future research, besides a questionnaire of RLS patients for VBI symptoms and obtaining brain and cervical MR angiography besides brain MR in these patients, it will be helpful to see the actual number of the patient population and the incidence of VBI and RLS to be seen together. In intravascular pathologies of the VA, endovascular management may be more appropriate, but as dense fibrosis

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exists around the kinking side in dolicoarteriopathies, new techniques that do not interrupt the blood flow may be more beneficial. Endovascular surgery has primarily taken the place of traditional surgical approaches in the treatment of intravascular pathologies. It will be crucial to understand the long-term effects of surgery and its influence on neurovascular pathways. Additionally, there is a need for randomized controlled trials to solidify the relationship between surgical outcomes and symptom relief.

Exploring the role of such surgeries in the broader context of neurovascular and sensorimotor disorders will also be valuable. Further investigations should aim to harness advanced imaging techniques for a deeper insight into post-surgical neurophysiological changes. Our findings point towards a promising direction for enhancing the treatment of VBI-related disorders, which merits continued scientific inquiry.

Expanding upon the innovative methodologies exemplified by Cekic et al., who successfully harnessed deep learning to segment and classify brain tumors [29]. We envisage a future direction for our neurosurgical strategies. Deep learning algorithms possess the transformative potential to identify vascular anomalies within the intricate milieu of the neurovascular landscape. By incorporating AI-driven technology into neurosurgical operations, we could substantially refine the real-time identification and management of vascular anatomies. This approach could be especially beneficial in vertebrobasilar and carotid dolicoarteriopathies and tubular stenosis, where precision is paramount [30]. Future studies might explore the feasibility of employing such algorithms to distinguish between pathological and normal vascular tissues during surgery, thereby augmenting the surgeon's precision and expanding the horizons for the treatment of refractory VBI.

Conclusion

In conclusion, RLS, alongside refractory VBI, necessitates a thorough evaluation of the vertebrobasilar system, mainly via MR angiography, to assess for potential contributory factors such as V1 segment dolicoarteriopathies. When symptoms are refractory to medical treatment and endovascular interventions are not viable, implementing microsurgical techniques targeting VA dolicoarteriopathies primarily for refractor VBI has demonstrated promising outcomes secondarily for RLS. Our study supports the potential of such micro-neurosurgical interventions to effectively rectify these conditions, substantially improving patient symptoms and indicating a significant step forward in managing these complex cerebrovascular disorders.

Compliance with Ethical Standards

Ethical approval: The Clinical Studies Ethics Committee of Bilecik Seyh Edebali University approved the study protocol and amendments (2/12, 03.30.2022) accordingly, with the clinical approval of the hospital and the local health authorities. The study was performed in accordance with the ethical standards of principles of the Declaration of Helsinki and Good Clinical Practices. After detailed information was provided, informed consent was obtained from all subjects.

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Authors' contributions: EC, ISD, and MEU: Conception and design, EC, and MEU: Data collection, EC, ISD, and MEU: Analyzed data, EC and MEU: Writing. All authors approved the final version of the article.

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