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Risk Factors for Vasovagal Reactions during Nonoperative Orthopedic Interventions in Outpatient Clinics: A Clinical Evaluation of 1,208 Patients

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Background: Vasovagal reactions (VVRs) are abnormal autonomic responses mediated by the vagus nerve. They can occur during or after interventional procedures and negatively impact patient care. The aim of this study was to evaluate the incidence of VVRs observed during nonoperative orthopedic interventions in outpatient clinics and to analyze the associated risk factors.

Methods: The data of 1,208 patients who underwent nonoperative orthopedic interventions at a single-center outpatient clinic between December 2023 and December 2024 were retrospectively analyzed. Patients were categorized into 2 groups based on the occurrence of VVR. The clinical data of both groups were analyzed to identify factors associated with VVRs.

Results: A total of 1,208 patients with a mean age of 54.7 years were included in the study. Among the 1,208 patients included, 51 cases of VVRs were reported (4.2%). The VVR group had a younger mean age (44.2 vs. 55.1 years, $p < 0.001$) and a higher proportion of females (74.5% vs. 59.2%, $p = 0.029$) compared to the non-VVR group. Mean visual analog scale (VAS) scores during intervention were higher in the VVR group (6.41 vs. 2.98, $p < 0.001$), and blood-injury-injection (BII) phobia was more common (39.2% vs. 1.8%, $p < 0.001$). Fasting time was longer in the VVR group (3.9 vs. 2.8 hours, $p = 0.003$). No significant differences were observed in hypertension, coronary artery disease, cerebrovascular disease, or asthma between groups ($p > 0.05$).

Conclusions: Younger age, female sex, higher VAS scores, BII phobia, and longer fasting times were the risk factors for VVRs associated with nonoperative orthopedic interventions.

Keywords: *Vasovagal reactions, Vasovagal syncope, Nonoperative orthopedic interventions, Outpatient procedures, Outpatient*

Vasovagal reactions (VVRs) are abnormal autonomic imbalances mediated by the vagus nerve, usually triggered by a stressful factor.[1-4] The term refers to arteriolar dilatation ("vaso-") and vagally mediated cardioinhibition ("vagal"), resulting in arterial hypotension and paradoxical bradycardia.[4-6] Trigger factors such as pain, fear, emotional distress, the sight of blood, fasting, prolonged standing, and visceral distention can induce an autonomic response, leading to decreased systemic vascular resistance, reduced venous return, and subsequent cerebral hypoperfusion.[2,3,7-9] Typical signs and symptoms of a VVR include dizziness or lightheadedness, pallor, palpitations, diaphoresis, blurred vision, nausea, vomiting, yawning, impaired hearing, and tinnitus.[1-4,8,9] If a VVR causes loss of consciousness, it is referred to as vasovagal syncope.[1,4,10] Although VVRs are generally self-limiting and resolve spontaneously, in some cases they may lead to unexpected risks and cause harm if not recognized and managed promptly. Sudden syncope

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and resulting falls, although uncommon, can result in injuries such as lacerations, concussions, and fractures.[1,4]

Outpatient procedures can induce VVRs. There are numerous reports in the literature indicating that outpatient procedures may be complicated by VVRs. Studies in the literature focusing on this topic are based on data from outpatient clinics in plastic surgery, dermatology, interventional neuroradiology, cardiology, algology, and blood donation units.[1-4,7,11-14] Furthermore, there is a study from an orthopedic center on VVRs during ultrasound-guided musculoskeletal injections.[15] However, to the best of our knowledge, no study has comprehensively examined the rate of VVRs in nonoperative orthopedic interventions commonly performed in the orthopedic outpatient clinic.

In our daily practice, we frequently observe that VVRs can develop during some interventions performed in the orthopedics outpatient clinic. This situation may pose a risk of trauma for patients and disrupt patient flow in a busy practice. The aim of this research is to investigate the incidence of VVRs in our orthopedic outpatient clinic and to explore the risk factors for VVRs associated with nonoperative orthopedic interventions commonly performed in the outpatient clinic, and to provide evidence for their prevention and management.

METHODS

The research was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ankara University Faculty of Medicine (No. i11-886-24). Informed consent was obtained from all individual participants included in the study.

This study was a retrospective analysis of prospectively collected data on patients who underwent nonoperative interventions in the orthopedic outpatient clinics of a secondary care hospital between December 2023 and December 2024. All invasive procedures, such as reduction maneuvers, injections, and suturing, were performed by a single orthopedic surgeon (MÖ) in the outpatient clinic. Some nonoperative interventions, such as suture removal or splinting without reduction, were performed by an experienced nurse. Fasting time was recorded before the intervention. Pain intensity during the intervention was assessed using the visual analog scale (VAS). VAS scores of 1–3 were classified as mild, 4–6 as moderate, and 7–10 as severe. After the procedure, a questionnaire was administered to collect data on patients' VAS scores during the intervention. In addition, all patients undergoing nonoperative interventions were systematically asked about VVR symptoms. In this questionnaire, patients were systematically asked about symptoms such as dizziness, blurred vision, amaurosis fugax, tinnitus, and nausea, whereas signs including pallor, diaphoresis, and syncope were recorded by the healthcare professional who performed the procedure (Supplementary Table 1). All patient-reported symptoms or clinician-observed signs that occurred during the intervention were recorded as VVRs.

All consecutive patients over the age of 18 who underwent nonoperative interventions in the orthopedic outpatient clinics were included in the study. The procedures were evaluated under the following categories: Jahss maneuver for metacarpal neck fractures, closed reduction and casting of distal radius fractures, upper extremity splinting without reduction, lower extremity splinting without reduction, suturing or suture removal, lateral epicondylitis injection, plantar fasciitis injection, intra-articular knee injection, and subacromial injection. The criteria for exclusion were as follows: (1) Patients under 18 years of age. (2) Patients who underwent orthopedic interventions in the emergency department or operating room. (3) Patients who received sedation or general anesthesia. (4) Patients with incomplete data (e.g., fasting time, or VAS score). The flowchart showing the selection of patients is presented in Fig. 1.

The baseline demographic data and comorbidities of the patients were retrospectively accessed from hospital

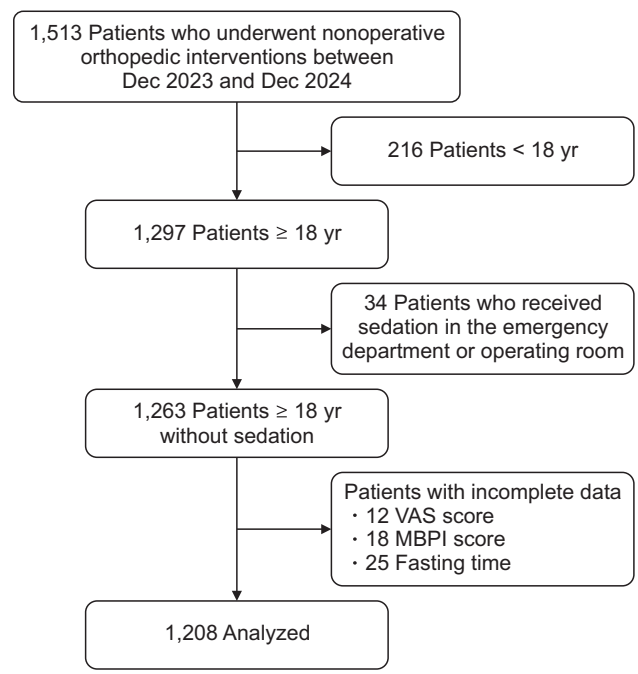


Fig. 1. Flowchart for the selection of patients. VAS: visual analog scale, MBPI: Multidimensional Blood/Injury Phobia Inventory.

medical records. Hospital archive data and diagnosis codes were used to determine the presence of hypertension, coronary artery disease, cerebrovascular disease, asthma, and chronic obstructive pulmonary disease (COPD) in patients. Clinical assessment of blood-injury-injection (BII) phobia was conducted using the Multidimensional Blood/Injury Phobia Inventory (MBPI). The MBPI was developed by Wenzel and Holt,[16] and the validity and reliability of the Turkish version were demonstrated by Ak et al.[17] MBPI was administered to all patients in our cohort. The association between the occurrence of VVRs and factors such as age, sex, pain intensity, fasting duration, and comorbidities was examined.

Statistical analysis was performed using IBM SPSS version 22.0 (IBM Corp.). Descriptive statistics were used to characterize demographic variables of patients. Mean and standard deviation was used to present descriptive statistics. Student's *t*-test was used to compare numerical data, while the chi-square test was used to compare categorical data between groups. Variables with a p-value < 0.15 in the univariate analyses were entered into a multivariate logistic regression model. The multivariate logistic regression analysis was performed using the backward elimination method to identify risk factors associated with VVRs. The p-values < 0.05 were considered statistically significant.

RESULTS

A total of 1,208 patients who underwent nonoperative orthopedic interventions were evaluated in this study. The patients consisted of 723 females (59.9%) and 485 males (40.1%) with a mean age of 54.7 years. Of the patients included, 51 (4.2%) developed VVRs. The types of nonoperative interventions and patient characteristics are presented in detail in Table 1. According to the types of nonoperative orthopedic interventions applied, the percentages of VVRs were observed as follows: Jahss maneuver for metacarpal neck fractures (n = 12, 35.3%), lateral epicondylitis injection (n = 7, 23.3%), closed reduction and casting of distal radius fractures (n = 11, 14.8%), plantar fasciitis injection (n = 6, 8.4%), suturing or suture removal (n = 10, 4.0%), intra-articular knee injection (n = 3, 1.0%), lower extremity splinting without reduction (n = 1, 0.7%), subacromial injection (n = 1, 0.6%), and upper extremity splinting without reduction (n = 0). The mean VAS score during the interventions was 3.1. The most painful procedures in terms of mean pain scores during the intervention were as follows: Jahss maneuver for metacarpal neck fractures, closed reduction of distal radius fractures, lateral epicondylitis injection, and plantar fasciitis injection. It was observed that the interventions with higher mean pain intensity scores also had higher rates of VVRs (Table 1).

Fifty-one cases of VVRs were recorded among 1,208 patients in this study. Dizziness (84.3%), pallor (80.4%),

Table 1. Nonoperative Interventions and Patient Characteristics in the Orthopedic Outpatient Clinic

	n	VAS score*	Age (yr)	Sex		Vasovagal
				Female	Male	Reaction
Jahss maneuver for metacarpal neck fractures	34	8.5 ± 0.9	24.9 ± 6.7	4 (11.8)	30 (88.2)	12 (35.3)
Lateral epicondylitis injection	30	7.1 ± 1.8	42.2 ± 13.2	22 (73.3)	8 (26.7)	7 (23.3)
Closed reduction and casting of distal radius fractures	74	7.5 ± 1.2	61.5 ± 7.6	56 (75.7)	18 (24.3)	11 (14.8)
Plantar fasciitis injection	71	6.0 ± 1.9	49.8 ± 12.1	53 (74.6)	18 (25.4)	6 (8.4)
Suturing or suture removal	248	2.8 ± 1.0	52.2 ± 15.1	129 (52.0)	119 (48.0)	10 (4.0)
Intra-articular knee injection	288	2.4 ± 1.0	65.4 ± 7.7	193 (67.0)	95 (33.0)	3 (1.0)
Lower extremity splinting without reduction	145	1.9 ± 0.9	49.1 ± 14.9	84 (57.9)	61 (42.1)	1 (0.7)
Subacromial injection	166	2.1 ± 0.8	60.3 ± 7.9	110 (66.3)	56 (33.7)	1 (0.6)
Upper extremity splinting without reduction	152	1.7 ± 0.9	45.4 ± 16.6	72 (47.4)	80 (52.6)	0
Total	1,208	3.1 ± 2.1	54.7 ± 15.1	723 (59.9)	485 (40.1)	51 (4.2)

Values are presented as mean±standard deviation or number (%).
VAS: visual analog scale.
*Measured during the procedure.

diaphoresis (74.5%), blurred vision (64.7%), and nausea (50.9%) were the most common symptoms. Amaurosis fugax was reported in 1 patient (1.9%), and tinnitus was reported in another patient (1.9%). Only prodromal symptoms developed in 50 out of 51 patients, and the presyncope symptoms regressed with the application of the Trendelenburg position. However, in 1 patient, loss of consciousness (syncope) occurred following the rapid onset of prodromal symptoms. In this patient, consciousness was restored after applying the Trendelenburg position. After regaining consciousness, the patient was transferred to the emergency department and received parenteral fluid therapy. The clinical findings of the VVRs are presented in Table 2.

Table 2. Clinical Findings of the VVRs (N = 51)

VVR	No. (%)
Dizziness	43 (84.3)
Pallor	41 (80.4)
Diaphoresis	38 (74.5)
Blurred vision	33 (64.7)
Nausea	26 (50.9)
Amaurosis fugax	1 (1.9)
Tinnitus	1 (1.9)
Syncope	1 (1.9)

VVR: vasovagal reaction.

The comparison of patient groups with and without VVR in terms of potential risk factors is presented in Table 3. The mean age of the patients in the VVR and non-VVR groups was 44.2 and 55.1, respectively. It was observed that the mean age in the VVR group was younger compared to the control group ($p < 0.001$). The proportions of female patients in the VVR and non-VVR groups were 74.5% and 59.2%, respectively ($p = 0.029$). The mean VAS score during the intervention was 6.41 in the VVR group, while it was 2.98 in the other group ($p < 0.001$). VVRs occurred more frequently in upper extremity interventions than in lower extremity interventions (6.0% vs. 2.0%, $p < 0.001$). The proportion of patients with blood injury and injection (BII) phobia was greater in the VVR group (39.2% vs. 1.8%, $p < 0.001$). Mean fasting time was longer in the VVR

Table 3. Comparison of Patient Groups with and without VVR during the Nonoperative Orthopedic Interventions

	VVR present (n = 51)	VVR absent (n = 1,157)	*p*-value
Age (yr)	44.2 ± 16.8	55.1 ± 14.9	< 0.001*
Sex			0.029*
Female	38 (74.5)	685 (59.2)	
Male	13 (25.5)	472 (40.8)	
VAS score	6.4 ± 2.9	2.9 ± 2.0	< 0.001*
Location			< 0.001*
Upper extremity	39 (6.4)	566 (93.6)	
Lower extremity	12 (2.0)	591 (98.0)	
BII phobia	20 (39.2)	21 (1.8)	< 0.001*
Fasting time (hr)	3.9 ± 2.4	2.8 ± 1.5	0.003*
Hypertension	12 (23.5)	332 (28.7)	0.424
Coronary artery disease	3 (5.9)	78 (6.7)	0.810
Cerebrovascular disease	1 (2.0)	45 (3.9)	0.481
Asthma or COPD	4 (7.8)	97 (8.4)	0.891

Values are presented as mean±standard deviation or number (%).
Pain intensity during the intervention was assessed using the VAS score.
VVR: vasovagal reaction, VAS: visual analog scale, BII phobia: blood-injury-injection phobia, COPD: chronic obstructive pulmonary disease.
*Differences were considered statistically significant for *p*-value < 0.05.
Student *t*-test was used to compare numerical data, while the chi-square test was used to compare categorical data.

Table 4. Multivariate Logistic Regression Model for the Occurrence of VVRs

Model	B	*p*-value	Odds ratio	95% CI
Age	–0.03	0.011*	0.97	0.95–0.99
Sex (female)	1.22	0.007*	3.39	1.39–8.21
VAS score	0.59	< 0.001*	1.80	1.53–2.12
BII phobia	4.72	< 0.001*	112.27	36.62–344.17
Fasting time	0.25	0.016*	1.28	1.05–1.57
Location (upper extremity)	0.89	0.044*	2.44	1.02–5.82

VVR: vasovagal reaction, VAS: visual analog scale, BII phobia: blood-injury-injection phobia.
*Statistically significant *p*-values (< 0.05).
Nagelkerke R^2 value for the model: 0.519.

group (3.9 hours vs. 2.8 hours, $p = 0.003$). However, there were no statistically significant differences in the proportion of patients with hypertension, coronary artery disease, cerebrovascular disease, asthma, or COPD between the 2 groups ($p > 0.05$).

Multivariate logistic regression analysis was performed to identify the risk factors associated with the occurrence of VVRs. The results indicated that younger age, female sex, higher VAS scores, BII phobia, and longer fasting times were the risk factors for VVRs associated with nonoperative orthopedic interventions (Table 4).

DISCUSSION

The pathophysiology of VVRs is complex, multifactorial, and not yet fully elucidated.[4-6] VVRs are most commonly characterized by hypotension, followed by paradoxical bradycardia.[3,4] In susceptible individuals, severe pain, emotional stress, fear, and similar triggering factors may lead to vasodilation through humoral or neural mechanisms.[5] Adrenal sympathetic activity rapidly increases during the presyncope phases.[6,18] Although epinephrine is a powerful vasoconstrictor of splanchnic vessels via alpha receptors, at high levels, it also exerts vasodilatory effects on skeletal muscle arterioles through beta receptors.[6,19] Due to vasodilation, systemic vascular resistance decreases, and venous return is reduced.[3-5] The most common explanation for paradoxical bradycardia following hypotension is the Bezold–Jarisch reflex.[4,5,20] This explanation suggests that excessive venous pooling leads to decreased blood pressure, which is detected by mechanoreceptors in the aortic arch, carotid sinus, and heart walls. These mechanoreceptors transmit the information to the nucleus tractus solitarius in the brain, eventually inhibiting the sympathetic response and increasing vagal tone, resulting in hypotension and bradycardia.[4,20]

It is known that VVR associated with outpatient interventions is not uncommon, with reported incidence rates ranging from 1% to 10.5% in the literature.[1-3] The existing studies primarily focus on other medical fields, such as plastic surgery, dermatology, interventional neuroradiology, and algology.[1-4,7,11-14] Additionally, a study conducted at an orthopedic center reported a 2.3% incidence of VVRs during ultrasound-guided musculoskeletal injections.[15] However, to the best of our knowledge, no study has comprehensively investigated the rate of VVRs in nonoperative orthopedic interventions commonly performed in the orthopedic outpatient clinic.

In our study, VVRs were reported in 51 out of 1,208 patients (4.2%). Although an optimal comparison is not possible due to the lack of similar studies on orthopedic outpatient interventions, the incidence of VVR appears to be consistent with that reported in other studies in the literature.[1-3] Dizziness, pallor, diaphoresis, blurred vision, nausea, vomiting, and heat/cold intolerance have been documented as the most common signs and symptoms of VVRs in the literature.[1-4,8,9] We found that dizziness (84.3%), pallor (80.4%), diaphoresis (74.5%), blurred vision (64.7%), and nausea (50.9%) were the most common symptoms of VVR, which is consistent with the literature. In our study, the incidence of syncope was lower compared to other studies in the literature.[1,2,4] Among the 51 cases of VVR, syncope was observed in only 1 patient (1.9%). Immediately interrupting the intervention upon the onset of presyncope symptoms and applying the Trendelenburg position may explain the low incidence of syncope in our study group.

Various risk factors have been linked to the occurrence of VVRs. According to several studies in the literature, a history of prior VVR and BII phobia are among the

most important risk factors for VVR.[2,4,12,21-23] BII phobia is a common psychiatric disorder, affecting approximately 3% to 4% of the general population, and is characterized by an intense, irrational fear and avoidance of situations involving blood, injections, injuries, or medical procedures.[21,24] Unlike other phobias, BII phobia is often associated with a vasovagal response, which can lead to dizziness or syncope upon exposure to feared stimuli.[21,25] Emotional stress and fear are known to be triggering factors that play a role in the pathophysiology of VVRs.[4,5] According to the literature, individuals with a history of VVRs are at a higher risk of experiencing future episodes.[4,22,23] In our study, the clinical evaluation of BII phobia was performed using the MBPI. This questionnaire was originally developed by Wenzel and Holt.[16] The validity and reliability of the Turkish version were established by Ak et al.[17] MBPI consists of 40 items, created by combining 4 types of stimuli (injection, hospital, blood, and injury) with 5 phobic response categories (fear, avoidance, anxiety, fainting, and disgust). Among the 1,208 patients included in our study, 41 (3.4%) were assessed as having BII phobia using this scale. VVRs occurred in 20 of these 41 patients during nonoperative orthopedic interventions. Of the 51 patients who experienced VVR, 20 (39.2%) had BII phobia. According to the multivariate logistic regression analysis in our study, BII phobia was observed to be the most significant risk factor for VVR. This finding is consistent with the literature. Patients should be evaluated for BII phobia or a history of past VVRs before orthopedic interventions, and caution should be taken regarding the risk of VVR.

Younger age and female sex have been reported as risk factors for VVRs in most studies.[2,26-28] Alboni et al.,[26] who published a review including data from 11,557 patients with vasovagal syncope, reported that the percentage of women was significantly higher than that of men (58% vs. 42%, $p = 0.03$). Romme et al.[28] reported that vasovagal syncope was more common in patients under 40 years than in those over 60 years. They also reported that prodromal VVRs were more common in younger patients and women than in older patients and men.[28] Jardine et al.,[6] in their laboratory study examining hemodynamic changes related to the vasovagal response, reported that the vasodilatory response was more common in younger patients. This condition makes younger patients more susceptible to VVRs. Al-Assam et al.[15] reported that VVRs were more common in patients under 65 years of age than in those over 65. They also stated that the rate of VVRs was higher in females compared to males (3.0% vs. 1.4%).[15] In our study, consistent with the literature, younger age and female sex were found to be associated with an increased risk of VVRs. Another important finding of our study was the relationship between pain intensity during the intervention and VVR. We observed that the likelihood of VVR was higher during interventions with severe pain intensity. This is supported by the fact that pain, like emotional stress and fear, is an effective trigger factor in the pathophysiology of VVR.[5]

Another noteworthy observation in our study was the significantly higher rate of VVRs during upper extremity interventions compared to lower extremity interventions (6.0% vs. 2.0%, $p < 0.001$). Painful procedures such as closed reduction were performed more frequently in the upper extremity. Additionally, direct visual exposure to the procedural field during upper extremity interventions may have contributed to this finding. Visual stimuli and emotional stress have been recognized as triggers for VVRs.[3-6] During upper extremity interventions, the ability to watch the procedure may have induced emotional stress, potentially contributing to higher pain scores and an increased incidence of VVRs.

The first recommended step in the treatment of VVRs is to remove the stimulus, meaning stopping the intervention immediately.[2,4,23] Rapidly reclining the patient into the Trendelenburg position is important to increase venous return and cerebral blood flow. This position involves placing the patient supine with the head lower than the feet, typically at an angle of approximately 30°.[2,4,29] It is recommended to use an adjustable examination table or an adjustable patient chair. If these are not available, laying the patient flat on their back on a stable surface is advised to achieve the Trendelenburg position.[2] Applying a cold compress to the forehead can help alert the patient.[2,4,23] Engaging the patient in conversation and providing reassurance are essential to alleviate their anxiety.[2] If these conservative measures are ineffective, parenteral fluid therapy should be initiated.[2,4,23] If adequate response is not achieved, treatment with a sympathomimetic such as ephedrine or an anticholinergic such as atropine may be necessary.[4,23] In our study, rapidly applying the Trendelenburg position was sufficient to resolve symptoms in 50 out of 51 patients who developed VVR. Only 1 patient was transferred to the emergency department and received parenteral fluid therapy. None of our patients required treatment with a sympathomimetic or an anticholinergic drug.

The study has several limitations. The main limitation of our study was its single-center design and the modest number of VVR events observed in our cohort. Another limitation was that patients who underwent orthopedic interventions in the emergency department were excluded.

A larger study with a multi-center design would be more informative. On the other hand, our study has several notable strengths. All invasive interventions were performed by a single orthopedic surgeon, ensuring high-quality procedural standards. To the best of our knowledge, this is the first comprehensive clinical study investigating the risk factors for VVRs associated with nonoperative orthopedic interventions commonly performed in the orthopedic outpatient clinic.

In conclusion, VVRs may occur during nonoperative orthopedic interventions in outpatient clinics and can be dangerous due to the risk of syncope and falls. Physicians performing these interventions should be aware of this possibility. Younger age, female sex, higher interventional pain scores, BII phobia, and longer fasting times were the risk factors for VVRs associated with nonoperative orthopedic interventions. Extra caution is needed before performing painful interventions in patients with a history of vasovagal episodes during previous medical procedures. For patients at high risk of VVRs, conscious sedation and monitoring during the intervention can be considered. If this option is not possible, the patient should be positioned in a setting that ensures safety from falling and allows for easy placement in the Trendelenburg position if necessary.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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SUPPLEMENTARY MATERIAL

Supplementary material is available in the electronic version of this paper at the CiOS website, www.ecios.org.

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