



Empty Nose Syndrome: The Case for “Functional Nasal Obstruction” as a Predisposing Risk Prior to Nasal Surgery

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Abstract

Purpose of Review Although empty nose syndrome (ENS) is axiomatically defined post nasal surgery, these patients present to otolaryngologists with complaints of nasal airflow dysfunction preoperatively. The critical question of how to resolve ENS should be in the preoperative assessment rather than focusing on interventions post nasal surgery. There are no proven factors from surgery that predict ENS post turbinate surgery. We review the latest literature on ENS and evaluate developing trends in the understanding of its pathophysiology and associations. This review seeks to develop a modern approach to the management of this recalcitrant condition.

Recent Findings Recent literature on ENS suggests possible psychogenic etiologies and associations, providing an avenue for treatment strategies. Previous theories of ENS pathogenesis regarding extent of turbinate surgery are not supported by airflow and radiologic assessments. Premorbid neurosensory alterations may explain why some patients, often with mental health comorbidities, present for nasal surgery without significant clinical findings and is a patient population predisposed to ENS.

Summary The concept of “functional nasal obstruction” or FNO, needs to become a diagnostic option for the clinician when assessing patients for nasal surgery. Patients identifying with ENS may be a population of patients with functional nasal obstruction, unrecognized and now after surgical efforts to relieve symptoms. The disorder underlying ENS should be considered an unrecognized risk factor in patient selection “prior” to nasal surgery rather than a postoperative complication “from” nasal surgery. Identifying this risk factor preoperatively is critical in avoiding subsequent morbidity. Further research into identifying “functional nasal obstruction” prior to nasal surgery should be undertaken as a priority over interventions after the ENS condition occurs.

Keywords Empty nose syndrome · Sinus surgery · Somatic symptom disorder · Depression · Risk factor · Functional nasal obstruction

Introduction

Empty nose syndrome (ENS) remains a controversial topic in contemporary rhinology notwithstanding an initial description almost 30 years ago [1]. It is a phenomenon

whereby patients present, after nasal surgery performed to relieve reported nasal obstruction, with postoperative continued or worsening paradoxical nasal obstruction despite a capacious nasal cavity. Debate remains not only around the optimal methods to manage ENS but also with regard to its

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etiology. Although the degree of nasal surgery is often implicated, studies do not show any difference in nasal airflow or resistance between patients who identify with ENS versus those with uneventful turbinate surgery [2]. Only studies using computational fluid dynamics models, largely from a single research center, have suggested differences [3–6]. The rarity of the condition has led to the lack of understanding of its pathophysiology and a multitude of reported treatments, issues embedded in this controversy.

In recent years, studies have identified potential pathophysiologic mechanisms inherent in ENS. These include a loss of trigeminal neural sensitivity, underlying anxiety/hyperventilation comorbidities or a possible mix of these producing symptoms. The definition of ENS is problematic as the presence of surgical attempts to improve the airway is part of the description. Therefore, it has become axiomatic that ENS patients present as a result of their surgery. However, the constellation of presenting symptoms of a patient later identifying as ENS may predict persistent symptomatology after nasal surgery. In this article, we review the latest literature and discuss the various proposed mechanisms and management philosophies of ENS as well as our own approach to this recalcitrant condition.

Historical Perspective

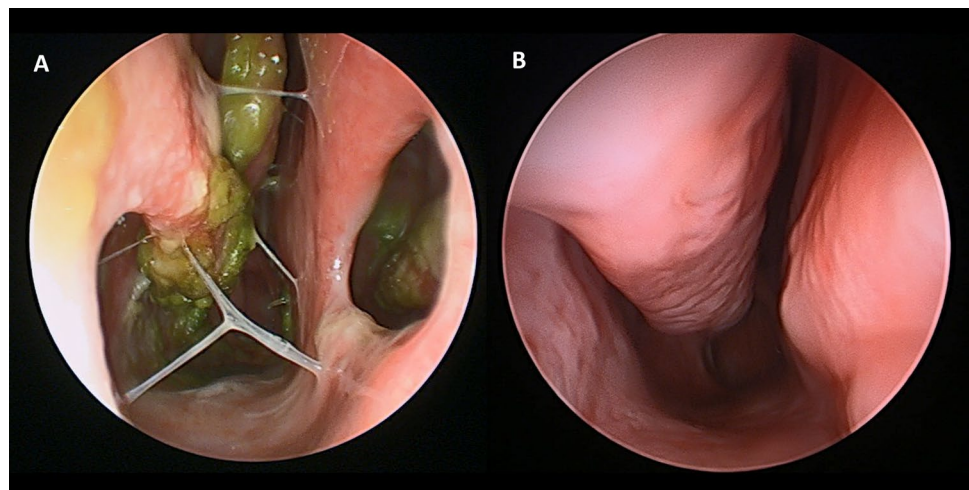
Described by Kern and Stenkvis at the Mayo Clinic in 1994, the term “empty nose syndrome” was originally used to depict the findings of tissue loss on sinus computed tomography (CT) associated with the hallmark symptom of paradoxical nasal obstruction [1]. This is classically attributed to aggressive inferior turbinate resection though symptoms have been described to occur after middle turbinate resection as well. ENS is not the same condition as atrophic rhinitis but the two are sometimes confused due to a similar

presentation of symptoms such as nasal obstruction, dryness, and pain. In particular, patients with atrophic rhinitis typically present with complaints of cacosmia and true crusting, with nasal cultures showing presence of the pathogenic organism *Klebsiella ozaenae*. ENS and atrophic rhinitis are now acknowledged as separate clinical entities (Fig. 1A–B) [7–9].

Nevertheless, the pathophysiology of ENS is still poorly understood. Many theories have been put forward but none sufficiently explain the phenomenon. Proposed etiologies include disruption of airflow dynamics and loss of airflow sensing neuroreceptors due to the alteration of nasal cavity anatomy from nasal surgery, resulting in the persistent sensation of nasal obstruction [3, 4, 9, 10]. Consequently, many of the treatments proposed for ENS have focused on restoration of tissue loss. However, assessments of inferior turbinate volume post turbinate reduction have shown no differences between ENS patients and patients with uneventful postoperative recovery [11]. Researchers have attempted to validate various diagnostic tests to confirm the diagnosis of ENS. These include a disease-specific questionnaire, the Empty Nose Syndrome 6-Item Questionnaire (ENS6Q), and the “cotton wool test” whereby the physician places a cotton wool ball into the patient’s nasal cavity to simulate the deficient nasal turbinate, [12] with an improvement in symptoms said to clinch the diagnosis. Common criticisms include the fact that the cotton wool test itself is inherently unblinded, while the ENS6Q includes questions that overlap with mental health symptoms.

Objective tests and measures have been proposed to define ENS. The presence of CT features of selective hypertrophy and mounding of nasal septal mucosa has been proposed as potentially diagnostic of ENS [11]. However, compensatory mucosal hypertrophy changes are expected post surgery and the ENS group assessed in those studies was more than twice as far out from their surgery compared

Fig. 1 Contrast of endoscopic findings between atrophic rhinitis and ENS. **A** Patient with atrophic rhinitis, presenting with nasal crusting, obstruction, and cacosmia. Endoscopic examination of the nasal cavity shows true crusting with nasal cultures confirming growth of *Klebsiella*. **B** Case example of ENS patient who initially presented with a sensation of nasal obstruction. Post inferior turbinoplasty, patient reported being distressed by persistent symptoms despite a normalized postoperative cavity with patent nasal airway



to the control group, which in itself may have resulted in more septal remodeling.

Significant questions remain about the proposed origins of ENS and there are many fundamental discrepancies with its original description. The proposal of ENS as a "complication of surgery" assumes a casual association of turbinate tissue loss and symptoms of nasal obstruction. It is often overlooked that this group of patients clearly presented to an otolaryngologist initially with symptoms of nasal obstruction but had persistent or worsening symptoms from simple septal and turbinate surgery performed in efforts to relieve the presenting nasal obstruction. Like the feelings of breathlessness in hyperventilation or the "air hunger" of anxiety, it is plausible that a "functional" nasal obstruction may be occurring in some patients with ENS. Surgical attempts to intervene not only fail to resolve symptoms but also lead to worsening symptoms and deterioration in mental health from unrealized expectations of benefit. Other inconsistencies exist in the theories of ENS (Box 1).

Box 1 Inconsistencies in the Theories of ENS

- What was the original diagnosis in ENS that required the nasal surgery? Did that etiology of nasal obstruction disappear to be replaced by a new one post surgery?
- Why is ENS only reported post nasal surgery for airflow obstruction? It is widely recognized that the condition is almost exclusively in this group and not in patients post sinus or tumor surgery who may have much greater turbinate tissue loss.
- Why are the anxiety, mental health, and hyperventilation symptoms so prominent in this group of patients and disproportionate to those with complete mechanical obstruction (e.g., grade 4 nasal polyps)?
- Why is sleep disturbance a major feature in ENS despite the open nasal passage, albeit feelings of obstruction, that should ensure nasal airflow mechanics are not contributing to sleep disordered breathing?

Traditional Treatments

The traditional management of ENS consists of an array of medical and surgical therapies including the usage of topical therapies, filler injections, submucosal graft implantation, and stem cell injection therapy [13, 14]. Surgical interventions generally aim to restore inferior meatal volume, based on the concept of inferior meatal volume loss and the resultant alteration of airflow sensation as the potential etiology of symptoms in ENS patients.

Unfortunately, none of the surgical intervention studies are controlled studies.

Topical Treatment

Medical therapy revolves around moisturization of the nasal lining, involving regular application of nasal saline irrigation and emollients [9]. Many of these ointments contain menthol, pine oil, and other trigeminal/transient receptor potential melastatin 8 (TRPM8) receptor agonists. These focus on relieving ENS symptoms via lubrication and recreating the cooling effect on the nasal cavity. High-volume irrigation is typically recommended due to improved distribution to the mucosal surfaces within the nasal cavity.

Submucosal Graft Implantation

Popularized surgical techniques primarily involve recreation of the inferior turbinate volume via submucosal implantation of the region of the inferior meatus with grafting materials [15, 16]. The array of grafts described includes acellular dermis, xenografts, cartilage, and synthetic implants such as silicone sheets and porous polyethylene (MedPor) [14]. The main disadvantages of this approach include risks specific to graft implantation such as graft extrusion and resorption.

Filler Injections

A less invasive surgical intervention for ENS is performed by injecting areas of the nasal cavity with a variety of fillers such as hyaluronic acid and carboxymethylcellulose [17, 18]. Similar to grafting techniques, filler injections attempt to restore nasal volume and bring the nose closer to a "physiological" state. This procedure is generally less preferred due to its inconsistent results, temporary effects, and possible tachyphylaxis.

Stem Cell Therapy

In an attempt to find a satisfactory treatment for ENS, Kim et al. evaluated the efficacy and safety of stem cell therapy as a novel method, using the injection of autologous stromal vascular fraction to both inferior turbinates [19]. Inflammatory markers were measured at baseline, with ENS patients showing an increase in markers such as interleukin (IL)-1 β , IL-8, and calcitonin gene-related peptide. Initial results show a decrease in inflammatory cytokine expression in treated patients, in particular that of IL-1 β and IL-8, though the

mean Sinonasal Outcome Test (SNOT)-25 scores of patients at 6 months after injection did not differ significantly from baseline.

The Potential for “Functional Nasal Obstruction” Exists in Otolaryngology

Despite the aforementioned methods previously used to manage ENS, the inconsistency of outcomes together with the lack of control groups and long-term follow-up in studies highlights the need to better understand the pathophysiology of ENS [20]. The potential for an ENS patient’s receptiveness to care, attention, and placebo effect is high in single-arm studies. Additionally, the strategies here are very disparate as they are aimed at a wide range of methods from moisturization, to occlusion of airflow and stem cell therapies.

Earlier literature reviews on ENS pathogenesis attributed the condition primarily to post-surgical impairment of the neurosensory system and trigeminal nerve function in the nasal cavity [10, 13]. However, close scrutiny of the evidence surrounding the pathophysiology of ENS has challenged this original assertion by Kern et al. [21]. It has been shown that patients who have undergone sinonasal tumor resection, involving extensive resection of nasal cavity structures, do not develop ENS [22, 23•]. Other studies looking at turbinate resection during radical sinus surgery for inflammatory diseases also echo this observation [24, 25]. The near absence of ENS in these patient groups with significantly greater alteration of their nasal cavities, as compared to simple turbinate procedures, questions the veracity of the “post-surgical” theory of ENS (Fig. 2A–E). A systematic review of studies examining the pathophysiology of ENS, comparing ENS patients to those with uneventful recovery post turbinate surgery, noted similar anatomical changes between groups and highlighted the presence of significant comorbid mental health disorders in patients with ENS [26••]. This relationship supports the proposal of a “functional” nasal obstruction condition

that must be present in some patients with nasal breathing symptoms that seek otolaryngologic assessment, in the same vein as functional hearing loss, functional dystonia, and functional epilepsy. There are examples of functional disorders, such as functional dyspepsia, that might have some subtle underlying pathophysiology beyond mental health interactions, but ultimately the mental health burden dominates symptomatology [27]. In ENS, there may be patients with subtle trigeminal nerve dysfunction but the symptom presentation is disproportionately dominated by deterioration in mental health. The diagnostic entity of “functional nasal obstruction” (FNO) must therefore surely exist within otolaryngology patients but the absence of its discussion in contemporary otolaryngology is remarkable.

There has been an increasing trend related to published ENS topics over the past 5 years, with a gradual shift from developing novel, further surgical interventions in ENS to identifying associations with psychological factors in attempts to direct therapy to the mental health comorbidities that burden these patients.

Mental Health and Psychogenic Associations

Recent studies acknowledge the association between ENS and mental health comorbidities such as depression and anxiety, highlighting a potential treatment pathway to explore [28, 29, 30•]. However, the causal relationship between the two is difficult to prove, as to whether it is ENS causing subsequent mental health issues or instead patients suffering from underlying FNO developing ENS after surgery. Determining whether these comorbidities predispose a patient to ENS, or vice versa, can be challenging. Patients with seemingly no psychiatric history preoperatively could potentially have an underlying personality disorder or undiagnosed depression and anxiety. These can manifest and exacerbate after the psychological stress of the initial sinonasal surgery, acting as a predisposing factor in ENS rather than as a result of.

An earlier study by Manji et al. looked at the functional and psychological burden of patients with ENS [29].

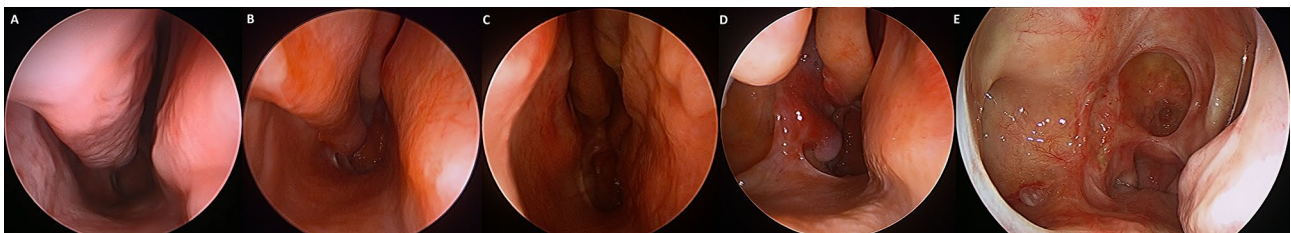


Fig. 2 Endoscopic examination of various nasal cavities, comparing the ENS patient to other patients with increasing extents of nasal surgery. **A** Inferior turbinate resection (ENS patient), **B** inferior turbinate resection (patient without ENS), **C** total inferior turbinectomy, **D** medial

maxillectomy, and **E** wide resection of skull base tumor. Despite the increasingly extensive loss of nasal cavity structures in patients B–E, none of these patients developed ENS as in patient A

Patients completed questionnaires assessing their psychological status which included the ENS6Q, the 9-item Patient Health Questionnaire for depression, and the 7-item Generalised Anxiety Disorder questionnaire [31]. ENS symptom severity was noted to have a strong positive correlation with depression, anxiety, and overall impairment in activities of daily living, and it was concluded that a multi-modal approach including cognitive behavioral therapy (CBT) may provide the most optimal treatment outcome.

It is interesting to note that patients with ENS often also fulfill the criteria for somatic symptom disorder [32, 33••]. As per the fifth edition of *The Diagnostic and Statistical Manual of Mental Disorders*, the diagnostic criteria for somatic symptom disorder include (A) one or more somatic symptoms that are distressing, (B) excessive thoughts, feelings, or behavior related to the somatic symptoms, (C) the state of being persistently symptomatic (typically more than 6 months) [34]. These symptoms are reminiscent of those typically seen in ENS patients and as such, it is not unreasonable to apply similar treatment modalities to those with ENS. Hyperventilation syndrome, characterized by excessive ventilation due to anxiety, has also shown to be comorbid in up to 77% of ENS patients [35] and should be considered a potential etiologic factor. This is sometimes described as occurring due to the lack of sensation of the nasal airway in ENS, though laryngectomized patients have not been noted to have hyperventilation despite having a lack of nasal airflow [36]. Feelings of dyspnea, shortness of breath, air hunger, and inability to breathe are common to anxiety disorders [37].

Other studies have also noted the association between ENS and an increase in psychological burden [28, 30•, 38–40], with various questionnaires being used to diagnose and assess the distressing effects of ENS, such as the ENS6Q and the SNOT-25 [1]. Validated instruments including the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory-II (BDI-II) have also been used to evaluate mental health comorbidities such as depression and anxiety [41, 42]. In particular, two separate research groups had similar findings of an increased prevalence of depression and mental health burden in ENS patients as compared to patients with chronic rhinosinusitis and chronic rhinitis [28, 30•]. The use of antidepressants and psychosomatic interventions such as CBT has shown potential benefit in ENS patients fulfilling the diagnostic criteria for somatic symptom disorder [33••].

Despite the mental health associations, it should be acknowledged that there is some evidence which suggests physical changes in the nasal anatomy of patients with ENS. Wu et al. showed that the nasal mucosa of ENS patients had a lower expression of TRPM8 receptors when compared to that of the control group [43]. These trigeminal receptors

have been implicated in the sensation of nasal patency, though it is uncertain if a reduced number of these receptors were already present preoperatively and the actual reason for the patient's sense of nasal obstruction rather than as a result of surgery.

The Diagnostic Utility of Functional Nasal Obstruction (FNO) in Contemporary Otolaryngology

As we mature in our understanding of ENS, the literature acknowledges an underlying mental health theme which should be incorporated into clinical practice. Given the evidence presented, it would be prudent to manage ENS as a predisposing risk factor in surgery rather than a postoperative complication. Patients at risk for the condition that we currently refer to as ENS should be considered suffering from “functional nasal obstruction” or FNO. This would be in line with other functional conditions in medicine. In keeping the term ENS, it implies a sense of pervasive injustice to the patient and vilifies the surgeon. The idea that “too much tissue was taken” or “the wrong turbinate procedure was performed” is not supported by studies on ENS patients compared to those with uneventful outcomes after turbinate surgery [26••]. Such a non-evidence-based assessment delivers a fatalistic outlook for the patient, condemns the prior surgeon's efforts to help, and reinforces the externalized locus of control that exists in many patients that blame a procedure for their ongoing symptoms. For many patients with FNO, the motivation for surgery includes unrealistic expectations of improved fitness, sleep, energy, and productivity after nasal surgery rather than simply relieving a blocked nose. FNO patients are at risk of having very high expectations from their turbinate surgery, and with the subsequent unrealized outcomes, the surgery becomes a trigger for mental health decline [44].

This shift in terminology might be more tactful to the patient with regard to future CBT and psychological support, avoids the fatalistic nature of the term “empty nose”, and be more evidence-based with regard to the condition's etiology. Another practical rationale for this change in mindset is that screening for FNO as a risk factor for ENS would involve a simple but robust process which allows the avoidance of surgery in at-risk patients, potentially obviating the devastating outcome of a patient identifying as ENS. While it would be ideal to identify patients with FNO preoperatively, we are aware that this is not always possible and patients may present postoperatively with ENS despite best efforts. Hence, our current approach to FNO can be dichotomized into preoperative and postoperative strategies.

Preoperative Approach

Care should be taken during history taking to screen for mental health comorbidities such as depression and anxiety, and the SNOT-22 questionnaire can be a useful screening tool. From our experience, at-risk patients tend to have a relatively higher score in the emotional subdomains. This produces a “right shift” of responses in the bottom of the SNOT-22, which reflects the disproportionate severity of psychosocial domains over nasal symptoms. To evaluate patients suitable for turbinate reduction, we commonly use “Ray’s Rules,” [26••] which refers to patients having the triad of (1) fluctuating or “cycling” nasal congestion, (2) postural congestion, and (3) subjective response to topical nasal decongestant. The above represents typical responses in patients with turbinate pathophysiology whereas patients who present without these are more likely to have FNO and be poor surgical candidates. The clinician should also be wary of a disproportional symptom burden compared to objective endoscopic findings. Other useful adjunctive investigations include rhinomanometry to obtain objective measurements of nasal obstruction, as well as CT of the paranasal sinuses to rule out occult sinus disease.

For example, in a patient with nasal obstruction having comorbid depression, equivocal endoscopy, and a “right shift” in the SNOT-22 as well as normal rhinomanometry and CT of the paranasal sinuses, one needs to weigh the risk-benefit ratio of surgery in a potential FNO patient. Opting for conservative measures over surgical management may avoid an at-risk FNO patient developing ENS from surgery. Caution should be taken with the patient harboring unrealistic expectations of improved fitness, sleep, energy, and productivity after nasal surgery as such patients are at risk of having high expectations with unrealized outcomes triggering a mental health decline. When preoperative patients ask about “the risk of ENS” from their procedure, an evidence-based answer should be given (Box 2).

Box 2 Example of What to Tell Patients Who Ask About “The Risk of ENS”

In response to a patient’s question about the risk of developing ENS from their nasal surgery, an evidence-based answer might be as follows:

“Unfortunately, the condition of ENS does exist after nasal surgery and is thought to be related to patients with nasal symptoms that are part of a broader mental health disorder such as anxiety and hyperventilation. For these patients, they have high expectations of what the nasal surgery will improve in their lives (fitness, sleep, energy, and productivity) and not unexpectedly, the surgery doesn’t improve their situation and often leads to

mental health decline. Whether a patient develops ENS, or not, is unrelated to the technique or extent of nasal surgery.”

And follow-up if required, especially if the surgeon believes that there is a discrepancy between symptoms and objective findings but not obvious FNO:

“And if you identify with this situation then you should be cautious about your decision to proceed with nasal surgery.”

Postoperative Approach

Postoperatively, our approach to patients with FNO is similar to the preoperative approach with detailed history taking and examination undertaken to rule out other obvious causes for persistent symptoms. Rhinomanometry would be particularly useful to confirm normal airway resistance and ensure that no objective nasal obstruction is present, so that patients can be appropriately counseled and reassured. The ENS6Q and SNOT-25 can also be used as a diagnostic aid in these circumstances, with the BAI and BDI-II used to screen for anxiety and depression.

Additionally, referral to a mental health professional should be recommended depending on the impact on the patient’s daily functioning. Such patients are often severely distressed by their symptoms and it would be circumspect to proceed with an early referral for potential CBT and to ensure that appropriate treatments are undertaken for any other comorbid depression and anxiety. Clinicians should try to refocus the patient away from the pervasive sense of injustice that they feel from their journey, which started with a presentation to an otolaryngologist prior to any surgery. We take caution in condemning any prior surgery and provide phrasing that the original nasal obstructive symptoms simply did not have a turbinate etiology (i.e., FNO), and expectation of benefit from surgery was misplaced.

Conclusion

Functional nasal obstruction (FNO) is a diagnostic entity that all surgeons should be aware of as a likely predisposing factor for ENS. Further research is required to ensure the otolaryngology community can identify these patients early and avoid ENS as a sequela after nasal surgery. The literature on ENS supports a strong association with mental health comorbidities compared to other pathologic causes of nasal blockage. A change in the approach from looking at this entity as a postoperative syndrome to that of a preoperative “functional” nasal obstruction should be considered, with potentially converging etiologies of impaired

trigeminal sensation, mental health comorbidities, and the unsuccessful nasal surgery as a stress event precipitating mental health decline.

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Declarations

Conflict of Interest Larry Kalish is on the speakers' bureau for Care Pharmaceuticals, Sequiris, and Meda Pharmaceuticals. Raymond Sacks is a consultant for Medtronic. Lu Hui Png has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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