A Numerical Model of the Influence of Maxillary Sinus Ostium Size on the Distribution of Nitric Oxide Concentration in the Nasal Cavity and Sinuses.

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Research

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Abstract

Objective

Using a numerical model, we aimed to study the influence of maxillary sinus ostium size variation on nitric oxide (NO) concentration distribution in the nasal cavity and sinuses and to determine the impact of differing sinus ostium size on sinusitis development and recurrence following sinus ostium opening surgery.

Methods

We obtained high-resolution computed tomography images of the nasal sinuses of a volunteer, following which we established a numerical model, determined NO concentration and air volume in the maxillary sinus on one side, then changed the maxillary sinus ostium size on that side, and finally established five models of sinus ostium of different sizes. Two sizes of sinus numerical models were established to determine effect of differing ostium size on the maxillary sinus cavity NO concentration distributions.

Results

A smaller sinus ostia size corresponded to lower NO concentration in nasal cavity and exhaled air; moreover, a concentration gradient was formed from sinus ostium to nasal cavity. A larger sinus ostia size demonstrated a lower NO concentration surrounding sinus ostium in the sinus cavity and formed a concentration gradient from ostium to cavity.

Conclusion

Constriction of the sinus cavity can lead to changes in NO concentration. Detection of NO concentration in nasally exhaled air can be used as an index to detect the patency of the maxillary sinus ostium. An excessive opening of sinus ostium leads to a decrease in NO concentration around sinus ostium, which is one of the main causes of persistent or recurrent inflammation in the maxillary sinus

Introduction

Chronic rhinosinusitis and fungal sinusitis are common diseases affecting humans. Serious cases may result in orbital or dental lesions, and even intracranial invasion, leading to serious complications [1]. The 2012 guidelines for the diagnosis and treatment of chronic rhinosinusitis suggests that functional endoscopic sinus surgery should be performed for chronic sinusitis with poor conservative treatment and impaired drainage around the sinus ostium. The purpose of such surgery is to open the blocked the sinus ostium, improve ventilation of the sinuses, and restore proper function of the mucociliary system. Whether the sinus ostium is open following surgery is the main determinant of prognosis [2]. The primary treatment method currently employed is nasal endoscopic sinus ostium opening and lesion removal [3]. However, some studies have found that in a subset of patients having undergone maxillary sinus surgery the drainage of the maxillary sinus remains poor and cannot be remedied, even though the sinus ostium
Nitric oxide (NO) plays a defensive role in the nasal cavity and sinuses, and exhibits antibacterial, antifungal and antiviral functions, promotes the secretion of nasal mucosa glands, maintains the wiggle mucous transport of nasal mucosa cilia, and regulates the vascular tension of nasal mucosa. NO is scarcely produced in the nasal cavity, and sinuses are the main source of nitric oxide in the upper airway. Due to the structural characteristics of the sinuses, the ostium is the key point of NO distribution and diffusion flow. Therefore, changes in size of the sinus ostium may affect the distribution and concentration of NO in the nasal sinus, leading to pathological changes of the nasal sinus and potentially to prolonged inflammation following operation on the sinus opening. A review of the literature revealed that a limited number of studies have been conducted worldwide in this field. In the current study, we aimed to understand the effect(s) of these aforementioned factors on the distribution and flow of NO in the nasal sinuses via numerical simulation.

The left maxillary sinus was selected as the research focus. A comparative model was set up based on changes to the left maxillary sinus ostium size, using the five size sinus numerical model that is established for investigating degrees of nasal NO concentration distribution and flow. Two sizes of sinus numerical models were established to study the effect of differing ostium size on maxillary sinus cavity NO concentration and distribution, and to further understand changes in nasal sinus orifice size, including the role of sinusitis and NO concentration distribution correlation.

Materials And Methods

1. Material acquisition: Obtain a CT image of a male volunteer: After a 30-minute rest, the volunteers underwent a high-resolution CT scan of the nose (Siemens Multi-Spiral CT) with a scan range of 30 mm above the skull base and throat. Between the horizontal levels, the layer width and the layer spacing are 0.39mm, the scanning window level is 20Hu, the window width is 2000Hu, and the resolution is 512*512 pixels. The imaging data in DICOM format is obtained.

2. Three-dimensional reconstruction:

   (1) Preliminary modeling of Mimics software: The CT scan for DICOM format image data import to Mimics17.0 medical image processing software (Materialise, Leuven, Belgium), isolated from the tip to the nasal airway images of nose pharynx ministry, because this section of the top part of the study of the size of the maxillary sinus change influence on nasal NO concentration distribution, therefore, in addition to the remove the ethmoid sinus and frontal sinus and sphenoid sinus, bilateral maxillary sinus cavity sinus structure, change the size of the left maxillary sinus ostium, extend the nasopharyngeal 2 times the length of the original, other structures shall not be altered, Five numerical models with diameters of 1mm, 3 mm, 6 mm, 8mm and 15mm were established. In the latter part, the influence of the change in the size of the maxillary sinus ostium on the distribution of NO concentration in the sinus cavity was studied. Therefore, two numerical models with diameters of the left maxillary sinus ostium of 6mm and 15mm containing bilateral maxillary sinus cavities were established, and the nasal cavity model was established and preliminarily smoothen, which was exported as STL data file.
(2) The Geomagic studio12.0 software smooth and curved surface generation: Mimics the STL format data file to import export to Geomagic studio12.0 (Geomagic, north Carolina, USA) software, generate smooth surface, export IGES format of the final model file.

(3) ICEM CFD software meshing: Import the final model file of IGES format exported by Geomagic studio12.0 into ICEM CFD software, and set the entrance and exit surface and boundary of the model (ie, the right front nose is set to inlet1, left front) The nostrils are set to inlet2, the nasopharyngeal part is set to outlet, the right maxillary sinus is set to right, the left maxillary sinus is set to left, the nasal airway is set to nose, and meshing is performed. The number of cells is 2.3 million, and the number of nodes is 405,000.) The meshed model is obtained and exported as the mesh file type (Figure 1).

3. Numerical simulation of gas flow field in nasal cavity

Fluent 15.0 was applied to calculate the airflow field of the nasal cavity. Set the airflow in the nasal cavity as turbulent and incompressible, and set the boundary conditions: (1) set the nasal airway wall as no slip and no permeability, that is, V=0m/s; (2) the front nostril is communicated with the outside world, set as the pressure inlet relative pressure P=0Pa; (3) the nasopharynx was set as the velocity outlet. The steady flow of airflow was Q=500ml/s.

Governing equation:

Continuity equation:

\[
\frac{\partial \rho}{\partial t} + \text{div} ( \rho \mathbf{u} ) = 0
\]  

(1) 

N-S equation:

\[
\frac{\partial (\rho \mathbf{u})}{\partial t} + \text{div} (\rho \mathbf{u} \mathbf{u}) = \text{div} (\mu \text{grad} \mathbf{u}) - \frac{\partial p}{\partial x}
\]  

(2)

\[
\frac{\partial (\rho \mathbf{v})}{\partial t} + \text{div} (\rho \mathbf{v} \mathbf{u}) = \text{div} (\mu \text{grad} \mathbf{v}) - \frac{\partial p}{\partial y}
\]  

(3)

\[
\frac{\partial (\rho \mathbf{w})}{\partial t} + \text{div} (\rho \mathbf{w} \mathbf{u}) = \text{div} (\mu \text{grad} \mathbf{w}) - \frac{\partial p}{\partial z}
\]  

(4)

and component mass conservation equation:
u, v, w are components of the velocity vector u in the x, y, and z directions, \( \rho \) is the air density, \( \mu \) is the dynamic viscosity, and \( p \) is the pressure.

The NO concentration of the maxillary sinus wall was used as the source, and the constant output of NO in the maxillary sinus wall was set to 0.1. No in the nasal cavity is mainly produced by the maxillary sinus wall. However, it is difficult to measure the concentration of NO in the maxillary sinus, so the concentration of NO in the maxillary sinus is set as the reference value (0.1, 0.3, 0.5, 0.7, 0.9, 1). We have Simulated and Calculated the distribution of NO in the nasal cavity corresponding to different reference concentrations, and the curve relationship between the concentration of NO in the maxillary sinus and in the nostril is established. The curve includes the relationship between the true concentration of NO produced by the maxillary sinus wall and the concentration of NO in the nostril. We select 0.1 to reflect the change rule of NO concentration in the nasal cavity and paranasal sinus.

Both air entering into the nasal cavity from the nostrils during inspiration and air entering from the nasopharynx during expiration were assumed to have zero concentration of NO for simplicity. Possible additional generation of NO by the nasal endothelium was not considered during analysis.

**Results**

1. Although there were differences in NO concentrations in maxillary sinus wall, no changes were observed in NO concentration gradient in PNSs (Figure 2).

2. For the NO concentrations of 0.1, 0.3, 0.5, 0.7, 0.9, and 1 in the left maxillary sinus wall, the corresponding NO concentrations in the left anterior nostril during the expiratory period were calculated, as given in Figure 3. The correlation curve showed that the NO concentrations in the maxillary sinus wall and anterior nostril had a linear positive relationship.

According to Table 1, when the airflow is constant the overall trend is that the larger the ostium, the higher the amount and concentration of NO exhaled from the ipsilateral anterior nostril.

Table 1 NO concentration of exhaled air from left anterior nostril in different sizes of left maxillary ostium
| Size of left maxillary sinus ostium (mm) | No content in left anterior nostril | Air volume of left front nostril | No concentration in left anterior nostril |
|----------------------------------------|------------------------------------|---------------------------------|-------------------------------------------|
| 1                                      | 2.17´10^9                          | 3.68´10^6                      | 0.62´10^3                                  |
| 3                                      | 5.27´10^9                          | 3.50´10^6                      | 1.50´10^3                                  |
| 6                                      | 12.45´10^9                         | 3.66´10^6                      | 6.65´10^3                                  |
| 8                                      | 13.47´10^9                         | 3.50´10^6                      | 9.81´10^3                                  |
| 15                                     | 19.23´10^9                         | 3.30´10^6                      | 27.2´10^3                                  |

2. Figure 4 shows a cloud map of NO concentration distribution in the left maxillary sinus ostium at 1, 3, 6, 8, and 15 mm during the steady-state expiratory period. The smaller the sinus ostia, the lower the NO concentration in the nasal cavity, vice versa. And a concentration gradient formed from the sinus ostium to the nasal cavity.

3. Figure 5 shows cloud map of NO concentration distribution in the left maxillary sinus ostium at 6 and 15 mm during the steady-state expiratory period. The larger the sinus ostium, the lower the concentration around the sinus ostium in the sinus cavity, forming a concentration gradient from the sinus ostium to the sinus cavity.

**Discussion**

Sinusitis is a very common disease resulting in significant negative impacts on quality of life and high costs. Proper ventilation is essential for sinus health, and the maxillary sinus ostium represents the only ventilating channel for the maxillary sinus. Also known as the maxillary sinus nasal passage, the maxillary sinus ostium is considered to be a key factor in the pathogenesis of sinusitis [9]. The most common course of treatment is to promote sinus drainage, such as via nasal congestion agent, sinus irrigation or other conservative treatment. Those with poor responses to these treatments are treated with endoscopic sinus opening to promote secretion excretion [10].

The maxillary sinus ostium is near the front of the boundary between the inner and top sinus wall, and is the only passage for the maxillary sinus to contact the outside environment. According to the literature, the maxillary sinus is mostly round or elliptical [11], and following the aforementioned opening surgery, it becomes basically circular [12]. Therefore, we built a circular model of the maxillary sinus ostium five numerical models based on varying ostium sizes, which were designed according to the existing literature. It has been published that the maximum sinus enlargement of the ostium is 15 mm in endoscopic surgery, thus this was set as the maximum size in the model [13]. It is currently considered that a sinus ostium > 6 mm is clearly open 6 months following operation [14-15], so sizes of 6 mm and 8 mm were also selected for the model. Normal maxillary sinus size is about 2-4 mm [16], thus an average diameter is 3mm [17], so this value was also chosen as well as a smaller representation of 1 mm.
During the expiratory period, the NO concentrations in the left nostril and MSs calculated using the proposed model showed that the NO concentration was 0.0268, which was within the range of actual concentrations (0.0018–0.4127) in the normal nose [2,18-21]. Therefore, the proposed numerical model is feasible, and the numerical simulation results are reliable.

Lesions around the maxillary sinus ostium, such as inflammation, nasal polyps, etc. cause the sinus to become smaller and limit ventilation drainage, thereby causing sinusitis caused by environmental changes in the maxillary sinus. From our numerical results, we can see that the size of the sinus ostium is positively correlated with the concentration of nasally exhaled NO, which is consistent with the study of Arnal [18 22] in which nasal nitric oxide concentration and sinus ostium obstruction was observed in patients with nasal polyps. Higher degrees of sinus occlusion result in decreased NO concentration in the nasal cavity. This is due to a reduction of the sinus ostium leading to limited NO discharge in the sinus and a decrease in NO discharge per unit time. When acute or chronic sinusitis occurs clinically, the mucous membrane of the sinus ostium swells, the sinus ostium narrows, and NO discharge in the sinus is limited. It has been shown in many studies that the concentration of nasally exuded NO at this time is lower than average [10,23-27]. According to the results of our numerical study, the concentration of nasal exhaled NO is positively correlated with the size of the sinus ostium, which indicates that the detection of nasally exhaled NO can be used to indirectly judge the degree of opening of the sinus.

The concentration of NO in the nasal cavity is positively correlated with the movement of cilia on the mucosal surface. The sinus cavity shrinks due to the decrease of NO flowing into the nasal cavity from the maxillary sinus, and the oscillating frequency of cilia slows down while the number of immobile cilia increases, and some even undergo cilia deformation [28]. On the other hand, NO mucus secretion of nasal mucosa promotes certain factors [10], for example: when NO concentration decreases so does mucus secretion, the formation of the mucus blanket is affected, the ability of nasal mucus cilia on the surface of the mucous membrane to perform transport drops, NO defensive ability decreases, acute rhinitis recovery may be slowed, NO concentrations may not improve long-term within the nasal cavity, and patients are even likely to develop chronic rhinitis.

In the past, the treatment of chronic and fungal sinusitides often required radical surgery, and currently functional endoscopic sinus surgery has become the primary surgical intervention. Endoscopic sinus surgery can achieve success by removing pathological tissue, patenting the ostium and improving drainage [29-30].

However, within such surgery to treat chronic sinusitis and fungal sinusitis, could greater opening of the maxillary sinus be a better treatment option and may it be easier for the maxillary sinus to become healthy with improved drainage? This results shown here indicate that a larger ostium exhibits greater influence on the same volume flow rate for the distribution of NO inside the nasal cavity and sinuses and around the ostium. Drainage in the maxillary sinus depends primarily on the ciliary system upon the mucosal surface. NO is a key factor to ensure normal operation of this system. Ciliary movement function of the nasal mucosal surface is impacted by the ciliary oscillation frequency and mucus cilia
transport speed. Higher NO concentrations lead to faster ciliary oscillation frequency on the surface of the mucosa, and increased mucociliary transport speed [28]. The mucilaginous blanket formed by sinuses epithelium and cilia swing on the surface of sinuses epithelium play the role of respiratory defense. Secretion of the epithelium and the frequency of cilia swing are positively correlated with NO concentration [31]. Combined with our results, enlargement of maxillary ostium will lead to decrease of NO concentration on the surface of the antral mucosa around the ostium, and closer proximity to the ostium is correlated with lower NO concentrations. If the opening of the sinus is too large, this may result in a low concentration of NO around the sinus, causing dysfunction of the ciliary transport system around the inside and outside of the sinus, and difficulty in discharging secretions, resulting in prolonged sinusitis and long-term retention of secretions.

In the study of Yuxiang et al. [14] investigating patient recovery after 476 lateral maxillary sinus opening surgeries, it was found that 15.95% of patients had a satisfactory opening of the maxillary sinus, but there was a long-term accumulation of purulent secretions in the maxillary sinus and the subjects remained symptomatic. However, there was a patient study group who did not undergo intervention of the maxillary sinus ostium to maintain its natural state, but only received intraoperative treatment for the lesion tissues blocking drainage around the sinus ostium. In this group, the sinus ostium was not blocked after surgery, and patients recovered well with no retention of maxillary sinus effusion. We speculate that this may be in part due to over-opening of the sinus ostium affected the distribution of NO concentration around the inside and outside of the sinus ostium, leading to both obstruction of the mucociliary transportation system in the sinus and drainage of postoperative sinus effusion. However, for patients who did not undergo intervention within the maxillary sinus ostium, the postoperative inflammatory relief of the maxillary sinus was ensured to maintain the physiological size of the sinus ostium, and normal operation of the ciliary transportation system in the maxillary sinus was maintained. Therefore, postoperative recovery was good for these patients, and no hydrops were found in their maxillary sinuses.

Of note, the antimicrobial effect of NO is concentration-dependent [32-36]. With expansion of the sinus ostium, NO concentration in the sinus cavity near the sinus ostium decreases, thus the antimicrobial effect decreases and the possibility of bacterial reproduction increases, which may be one of the causes of repeated inflammation after functional nasal endoscopic surgery.

Conclusion

It appears that in its natural state the maxillary sinus ostium is not as open as possible, and while some believe that a larger opening of the maxillary sinus leads to more favorable drainage, our research does not agree with this assumption. When the maxillary sinus opening is too large—which not only affects the concentration distribution of NO around the sinus ostium, but also the NO concentration in the nasal cavity—this may cause corresponding physiological and pathological changes. Therefore, clinical operation should aim not to enlarge the maxillary sinus after opening, and instead should try to avoid postoperative shrinking of the sinus ostium and atresia.
Declarations

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of The Second Affiliated Hospital of Dalian Medical University (2020 no.035).

Consent for publication

All presentations of case reports have consent for publication.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Author Contributions

Conceptualization, GUO Yan. and YU Shen; methodology, GUO Yan.; software, YU Shen.; validation, YU Shen, GUO Yan. and JIN Wen; formal analysis, GUO Yan. and YU Shen.; investigation, CUI Yu-yue and Yang Yi; resources, CUI Yu-yue and Yang Yi; data curation, YU Shen, GUO Yan. and JIN Wen; writing—original draft preparation, GUO Yan; writing—review and editing, GUO Yan; visualization, YU Shen, GUO Yan. and JIN Wen; supervision, WANG Ji-zhe and SUN Xiu-zhen.; project administration, SUN Xiu-zhen; funding acquisition, SUN Xiu-zhen. All authors have read and agreed to the published version of the manuscript.

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**Figures**

![Model meshing](image)

**Figure 1**

Model meshing
| NO concentration in maxillary sinus wall | NO concentration in maxillary sinus wall |
|----------------------------------------|----------------------------------------|
| 0.01                                   | 0.1                                    |
| 0.3                                    | 0.5                                    |
| 0.7                                    | 0.9                                    |

**Figure 2**

Coronal distribution of nitric oxide concentrations in the nasal cavity and maxillary sinus
Figure 3

Line chart of NO concentrations in the left anterior nostril and left MS.
### Figure 4

A cloud map of NO concentration distribution in the left maxillary sinus ostium at 1, 3, 6, 8, and 15 mm during the steady-state expiratory period.
| The distribution of NO concentration in the middle nasal passage and maxillary sinus of 6mm sinus at the volume flow rate of 500ml/sec | Distribution of NO in the middle nasal passage and maxillary sinus of 15mm sinus ostium |

**Figure 5**

Cloud map of NO concentration distribution in the left maxillary sinus ostium at 6 and 15 mm during the steady-state expiratory period.