# Cone Beam Computed Tomography in observing the presence and location of canalis sinuosus

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**Abstract.** – OBJECTIVE: Cone Beam Computed Tomography (CBCT) was used to observe and describe the distribution of canalis sinuosus (CS) in the Chinese population and the location of CS in the maxillary alveolar bone, so as to help oral surgeons evaluate the intraoperative risk and prognosis before maxillary surgery and reduce the complications caused by the injury of this structure in anterior surgery.

**PATIENTS AND METHODS:** CBCT images of 600 patients admitted from 2021 to 2022 were collected to observe the anatomical structure of CS in the maxillary region. The following parameters were recorded: age, sex, number of CS, left and right distribution of CS, CS diameter, and location. Statistical analysis was performed on all of the collected data.

**RESULTS:** The discovery rate of CS in this study was 59.75%, and it is commonly found in the lateral incisor area (64.82%). No significant difference can be found in the presence and number of CS in different gender and age groups (p>0.05).

**CONCLUSIONS:** The use of high-resolution CBCT before implantation is of irreplaceable significance in the diagnosis and analysis of CS, which is conducive to reducing implantation complications and failure rate. The incidence of CS was independent of age or sex, while the location of CS was statistically significant.

*Key Words:* CS, Dental implant, CBCT.

### Introduction

The canalis sinuosus (CS) is an inconspicuous structure containing neurovascular elements, initially reported by Jones in 1939<sup>1,2</sup>. CS originates

from the infraorbital canal, containing the upper alveolar blood vessels and nerves<sup>3</sup>. Initially, it traverses along the orbital floor, passing through the region below the infraorbital foramen, then turns medially and bends downward to travel along the front wall of the maxillary sinus to the lateral wall of the nasal cavity, while emitting numerous small branches that extend toward the teeth, alveolar bone and the incisive foramen. CS primarily provides sensory and blood supply to the anterior maxillary teeth region<sup>4,5</sup>.

In numerous research papers<sup>6,7</sup> and textbooks, the incidence of CS is relatively common, and it is regarded as an anatomical structure rather than a variation. However, some clinical doctors lack awareness of this structure, often mistaking it for a periapical radiograph of the maxillary teeth and incorrectly diagnosing it as periapical disease<sup>7,8</sup>.

Complications resulting from CS damage due to surgical or diagnostic errors in the anterior maxillary region have been reported in clinical practice, with implant failure being the most common<sup>1,2,9</sup>. This is likely attributable to the frequent placement of dental implants on the palatal side of the alveolar ridge in clinical practice<sup>10</sup>, where CS is commonly distributed<sup>11</sup>, rendering it susceptible to damage during implantation. Common symptoms experienced by patients after implant placement in these cases include pain, temporary or permanent sensory abnormalities, potential bleeding leading to compromised bone integration, and local infection<sup>2,7,10</sup>. While most patients' sensory abnormalities disappear after implant removal<sup>9,12,13</sup>, a few patients still experience persistent sensory abnormalities even after removal<sup>14</sup>.

Hence, when planning surgery in the anterior maxillary region, a comprehensive clinical and radiographic examination must be conducted to minimize the likelihood of surgical failure and complications<sup>15</sup>. In comparison to periapical and panoramic radiographs, Cone Beam Computed Tomography (CBCT) offers higher resolution, lower radiation exposure, and the capability for three-dimensional analysis at varying levels. It is considered the optimal method for pre-surgical diagnosis of anatomical structures, and utilizing CBCT to assess the surgical site prior to surgery contributes to precise diagnosis and reduction of surgical complications and risks<sup>3,15-18</sup>.

The aim of this study is to use CBCT to observe the presence, morphology, and location of CS in the maxillary region, and to measure its diameter and the distance between the palatal opening of CS and buccal cortical bone (BCB), nasal cavity floor (NCF), alveolar ridge (ARC), and incisive foramen in relation to gender and age. This will help to better analyze this anatomical structure during surgical procedures, thereby reducing the incidence of intraoperative and postoperative complications and surgical failure caused by CS damage.

### Patients and Methods

# General Information

We conducted a retrospective analysis on a random sample of patients with CBCT images taken between April 2021 and April 2022. Exclusion criteria included non-permanent dentition, prior sur-

gery or bone transplantation in the anterior maxillary region, trauma, pathological lesions, missing teeth, or developmental abnormalities (e.g., cleft palate, supernumerary teeth) in the anterior maxillary region, previous or ongoing orthodontic treatment, unclear or insufficiently thick CBCT images (observation layer thickness <200 um). Ultimately, 159 patients' CBCT images met the criteria. The study recorded the following parameters: gender, age, CS distribution (left or right), CS morphology, palatal opening diameter of CS on the alveolar ridge, relationship between CS structure with palatal opening diameter >0.3 mm and teeth, and distance between CS at the palatal opening of the alveolar ridge and buccal cortical bone (BCB), nasal cavity floor (NCF), alveolar ridge (ARC), and incisive foramen.

### **Collection Tools**

All CBCT images were obtained using Carestream YIAL006 equipment (Carestream Inc., New York, USA), with a minimum layer thickness of 200  $\mu$ m. CS Imaging Patient Browser 7.0 (Carestream Inc., New York, USA) was used for observation.

# **Observation Procedure**

The selected patients were randomly assigned numbers, and their gender and age were recorded. The CBCT images were analyzed in three steps: first, the presence of CS, the number, and the distribution (on the left sides or the right) were observed. Second, the morphology of CS was recorded (according to Von Arx's<sup>10</sup> method, which classifies CS into vertical, Y-shaped, and curved types, as shown in Figure 1). Thirdly, the palatal



**Figure 1.** Three types of CS morphology. **A**, Vertical type (runs perpendicular to the bottom of the nose to the alveolar ridge). **B**, Y-shaped type (originates from CS and other nasal floor branches). **C**, Curved type (curves downward toward the alveolar ridge).



Figure 2. Measurement method of CS opening diameter.

opening diameter was measured at the endpoint on the alveolar ridge where the CS canal opens (only CS structures with openings on the palatal side of the alveolar ridge and an opening diameter greater than 0.3 mm were recorded). Finally, the relationship between CS and teeth was recorded (central incisor area, lateral incisor area, canine area, first premolar area, second premolar area, and distant area of the second premolar), and the three-dimensional situation of CS was recorded (the distance from the palatal opening of CS to BCB, NCF, ARC, and incisive foramen).

# Measurement Method

1. CS diameter: find the palatal opening on the alveolar ridge in the coronal section, and use the axial cursor (yellow) perpendicular to the long axis of the CS canal to measure the buccolingual and mesiodistal diameters at the opening in the axial section. Record the average value, as shown in Figure 2.  Record the three-dimensional situation of CS: in the axial section, place the CBCT measurement software cursor at the palatal opening of CS on the alveolar ridge, adjust the sagittal section direction (blue) to make the section vertical to the dental arch, and measure the distance between the opening and the long axis of the incisive foramen - A. Finally, on the sagittal section (blue), measure and record the distance from the palatal opening to nasal cavity floor (NCF) - B, buccal cortical bone (BCB) - C and alveolar ridge (ARC) - D as shown in Figure 3.

# Analysis Method

The experimental data was collected and organized into an Excel database. All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). *p*<0.05 was considered statistically significant.

# Results

We collected CBCT images from 600 patients. According to exclusion criteria, 159 patients were included in the study [93 female (58.49%) and 66 male (41.51%)].

# Existence of CS

A total of 95 patients (59.75%) were observed to have CS structures with openings on the palatal side of the alveolar ridge and an opening diameter greater than 0.3 mm. Among them, there were 37 males (56.06%) and 58 females (62.37%).



Figure 3. Three-dimensional positioning method for CS opening.

Table	I. Number	of CS	in ea	ch age	group.
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		With or Without CS			<b>T</b> ( )
	Age		Without	With	count
Age group	12-19	Count	17	23	40
001		Percentage in this age group (%)	42.5	57.5	
	20-29	Count	11	19	30
		Percentage in this age group (%)	36.7	63.3	
	30-39	Count	10	15	25
		Percentage in this age group (%)	40	60	
	40-49	Count	11	20	31
		Percentage in this age group (%)	35.5	64.5	
	50-59	Count	10	13	23
		Percentage in this age group (%)	43.5	56.5	
	Over 60	Count	5	5	10
		Percentage in this age group (%)	50	50	
Total		Count	64	95	159
		Percentage in this age group (%)	40.3	59.7	

No statistically significant difference can be seen in the existence of CS between genders. (p=0.424 > 0.05).

The number of CS in each age group is shown in Table I. The highest detection rate of CS was in the 40-49 age group, but no statistically significant difference can be seen in the existence of CS among different age groups (p=0.960 > 0.05).

### Number of CS

The association between the number of CS and gender is presented in Table II. There is no statistically significant difference in the number of CS across various genders and age groups (p=0.600 > 0.05, p=0.510 > 0.05).

# Distribution of CS

# Left-right distribution of CS

Within the group of patients with CS structures featuring openings on the palatal side of the alveolar ridge and an opening diameter exceeding 0.3 mm, 24 patients (25.26%) exhibited CS structures on the right side, 40 patients (42.11%) on the left side, and 31 patients (32.63%) on both sides. There were no statistically significant differences in the left-right distribution of CS among various genders and age groups (p=0.419 >0.05 and p=0.916 >0.05, respectively).

Out of the 162 observed CS structures with openings on the palatal side of the alveolar ridge and an opening diameter exceeding 0.3 mm, 92 (56. 79%) were located on the left side and 70 (43.21%) on the right side. The difference in left-right distribution of CS was not statistically significant.

### Distribution of CS by tooth

Figure 4 illustrates that the lateral incisor area had the highest distribution of CS (34.57%), followed by the central incisor region (30.25%) and the canine region (20.37%), while the second premolar and its mesial and distal regions exhibited the lowest distribution. There were no statistically significant differences in the distribution of CS by tooth among different genders (p=0.144 > 0.05).

Table II. Relationship	between number	of CS and gender
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	Number of CS	Male count	Female count	Total
Distribution of male and female count	0	29	35	64
	1	17	33	50
	2	11	19	30
	3	5	4	9
	4	3	2	5
	5	1	0	1
Total		66	93	159



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Figure 4. Proportion of CS distribution in different dental position regions.

# Morphology of CS

Among the 162 CS structures with openings on the palatal side of the alveolar ridge and an opening diameter greater than 0.3 mm that were observed, the majority of CS structures had a curved morphology (64.81%), followed by a vertical morphology (31.28%), and Y-shaped morphology was the least common (3.70%). The relationship between the morphology of CS and gender can be seen in Table III. No statistically significant difference can be seen in the morphology of CS among different genders and age groups (p=1.0 > 0.05, p=0.989 > 0.05, respectively).

# Diameter of CS

Among the 162 CS structures with openings on the palatal side of the alveolar ridge that were observed, the average opening diameter of CS was  $0.887\pm0.2737$  mm. No statistically significant difference can be found in the diameter of CS among different genders (p=0.534 > 0.05) or age groups (p=0.869 > 0.05).

# Three-Dimensional Position of CS

The average distance from the palatal opening of CS to BCB, NCF, ARC, and the long axis of the incisal canal can be seen in Table IV.

Statistically significant differences can be found in the distance from the palatal opening of CS to BCB (p=0.022 < 0.05) and ARC (p=0.014 < 0.05) among different genders, with the distance being smaller in females than in males. Statistically significant differences can also be found in the distance from the palatal opening of CS

	Curved	morphology	Vertical morphology		Y-shaped morphology	
Number of CS	Left	Right	Left	Right	Left	Right
Gender						
Female	35	24	15	14	2	1
Male	26	20	12	10	2	1
Total	61	44	27	21	4	2
Total (percentage)	105 (6	64.81)	51	(31.48)	6	(3.70)

Table III. Relationship between the morphology of CS and its left-right distribution by gender.

	The average distance (mm)	Males (mm)	Females (mm)
BCB	$9.027 \pm 3.14$	$9.665 \pm 3.150$	$8.529 \pm 3.057$
NCF	$11.994 \pm 4.137$	$12.155 \pm 4.982$	$11.868 \pm 3.358$
ARC	$11.433 \pm 3.476$	$12.207 \pm 3.809$	$10.829 \pm 3.080$
Long axis of incisal canal	$11.212 \pm 4.485$	$11.586\pm4.932$	$10.921 \pm 4.108$

Table IV. The average distance to the palatal opening.

Buccal cortical bone (BCB), nasal cavity floor (NCF), alveolar ridge (ARC).

to BCB (p=0.013 < 0.05), ARC (p=0.014 < 0.05) among different age groups, with the distance becoming smaller as the age group increased.

No statistically significant difference can be found in the distance from the palatal opening of CS to NCF (p=0.678 > 0.05) the long axis of the incisal canal (p=0.406 > 0.05). Among different genders or age groups. No statistically significant difference can also be found in the distance between the palatal opening of CS and the long axis of the incisal canal among different genders (p=0.362 > 0.05) or age groups (p=0.687 > 0.05).

### Discussion

### Results and Analysis

# Presence of CS

After screening CBCT images of 600 patients, 159 patients were included, among whom 95 had a palatal-side alveolar ridge opening with a diameter exceeding 0.3 mm. The overall population prevalence of CS was 59.75%. The prevalence of CS varies widely among similar studies in different populations, for example, Von Arx et al<sup>10</sup> (27.8%), Tomrukçu and Köse<sup>16</sup> (34.66%), La Encina et al<sup>19</sup> (50%), Anatoly et al<sup>20</sup> (67%), Orhan et  $al^4$  (70.8%), and De Oliveira-Neto et  $al^{21}$  (80%). The prevalence of CS in this study was close to that of Machado et al<sup>11</sup> (52.1%). Some studies<sup>10,21</sup> have reported low prevalence rates of CS, such as De Oliveira-Neto et al<sup>21</sup> (15.7%) and Von Arx et al<sup>10</sup> (27.8%), probably due to the fact that they only measured CS structures with diameters greater than 1 mm or openings on the palatal side with diameters greater than 0.5 mm. Other studies<sup>4,21</sup> have reported high prevalence rates, which may be due to the fact that all CS structures were recorded and analyzed without limiting the opening position and diameter. It is also possible that the different studies used different slice thicknesses. Anatoly et al<sup>20</sup> found that the thinner the slice thickness (they changed the CBCT scan slice thickness from 0.5 mm to 1 mm to 3 mm), the better the visualization of CS in the images with different slice thicknesses.

Similar to this study, most of the literature describes no statistically significant difference in the prevalence of CS between males and females, such as Von Arx et al<sup>10</sup>, De Oliveira-Neto et al<sup>21</sup>, and Orhan et al<sup>4</sup>, but there are also some studies that differ, such as Anatoly et al<sup>20</sup> who found a lower prevalence of CS in males than in females, Machado et al<sup>11</sup> and Tomrukçu and Köse<sup>16</sup> who found a lower prevalence of CS in females than in males, which may be due to differences in ethnicity and region. Overall, differences in the prevalence of CS may be due to methodological differences (slice distance, CBCT scanner type and parameters, inclusion/exclusion criteria, etc.), as well as ethnic differences.

This study found no statistically significant difference in CS prevalence among different age groups. Among the six age groups, the highest prevalence of CS was found in the 40-49 years (64.5%) group. Most studies, such as Von Arx et al<sup>10</sup>, Machado et al<sup>11</sup>, De Oliveira-Neto et al<sup>21</sup>, and Aoki et al<sup>22</sup> record that no statistically significant difference was found in the prevalence of CS among different age groups. However, in terms of the relationship between age group and CS prevalence, studies by Von Arx et al<sup>10</sup> and Orhan et al<sup>4</sup> have found that the highest prevalence of CS is often in the 50 years and older group. In this study, the highest prevalence of CS was found in the 40-49 years group. Analysis suggests two potential reasons for this difference: ethnic variations within the region and disparities in sample inclusion/exclusion criteria. This study employed stricter exclusion criteria than other studies, mandating the absence of missing teeth or other lesions in the anterior region. Consequently, most patients over 50 years of age did not meet the inclusion criteria, leading to a smaller sample size that may not accurately reflect the situation of this age group in the population.

# Number of CS

In this study, a total of 162 CS structures with an opening diameter greater than 0.3 mm on the palatal side of the alveolar ridge were found, and no statistically significant difference can be found in the number of CS structures among different genders and age groups. Most of the literature, such as Orhan et al<sup>4</sup>, Von Arx et al<sup>10</sup>, and De Oliveira-Neto et al<sup>21</sup>, documents the same conclusion.

# Distribution of CS

# Left-Right distribution of CS

No statistically significant difference was seen in the left-right distribution of CS structures among different genders and age groups in this study, which is consistent with the findings of Von Arx et al<sup>10</sup> and Orhan et al<sup>4</sup>.

Of the 162 CS structures found with an opening diameter greater than 0.3 mm on the palatal side of the alveolar ridge, there were 92 (56.79%) on the left side and 70 (43.21%) on the right, and no statistically significant difference was seen in the left-right distribution of CS.

# Relationship between distribution of CS and Tooth Region

This study revealed that CS structures were predominantly distributed in the lateral incisor region (34.57%), followed by the central incisor (30.25%) and the canine region (20.37%). The second premolar and its distal region exhibited the lowest distribution of CS structures, consistent with findings by Tomrukçu and Köse<sup>16</sup>. Variations exist in the distribution of CS structures and their relationship to tooth position across different studies for example, Von Arx et al<sup>10</sup> reported a predominant distribution of CS structures in the central incisor region, whereas De Oliveira-Neto et al<sup>21</sup> and Sekerci et al<sup>23</sup> found that CS structures were mostly distributed in the central incisor and canine regions. Ghandourah et al<sup>13</sup> noted a majority distribution of CS structures in the central incisor region among adults, compared to adolescents, where they were mainly distributed in the central incisor and canine regions. These variations may be attributed to ethnic or methodological differences. Nonetheless, it is indisputable that CS structures are predominantly distributed in the anterior teeth area. Consequently, meticulous CBCT analysis of the implantation area is essential in clinical practice to minimize complications and implant failures resulting from CS damage during and after surgery.

# Morphology of CS

According to the method proposed by Von Arx et al<sup>10</sup>, CS structures can be divided into three types: curved, vertical, and Y-shaped. In this study, it was found that the most common was the curved type and the Y-shaped type was the least. These findings are consistent with the studies of Von Arx et al<sup>10</sup> [curved type (56.7%) > vertical type (41.8%) > Y-shaped type (1.5%)] and Tomrukçu and Köse<sup>16</sup> [curved type (69.15%) > vertical type (29.16%) > Y-shaped type (4.67%)].

### Diameter of CS

Of the 162 CS structures analyzed, the average diameter was 0.787±0.2737 mm, with no statistically significant differences observed in the diameter of CS structures across different genders and age groups. Discrepancies were noted in comparison to other studies regarding the average diameter of CS structures, for instance Von Arx et al<sup>10</sup> (1.31 mm), Machado et al<sup>11</sup> (1.19 mm), Tomrukçu and Köse<sup>16</sup> (1.3 mm), De Oliveira-Neto et al<sup>21</sup> (1.4 mm), and Sekerci et al<sup>23</sup> (1.2 mm). These variations could stem from differences in the collection and analysis methods, with some studies<sup>10,23</sup> only including CS structures with a diameter greater than 0.5 mm or even 1 mm, and measuring the diameter at different locations. Ethnic differences may also play a role, given that the anatomical volume of individuals of different ethnicities varies. Nevertheless, no statistically significant differences were observed in the diameter of CS structures among different age groups and genders, aligning with the majority of existing literature.

# Analysis of CS Palatal Opening

### CS palatal opening and age group

No statistically significant difference was observed in the distance between the CS palatal opening and the NCF among different age groups in this study. However, a statistically significant decrease was observed in the distance from the CS palatal opening to the BCB and ACR with increasing age. Tomrukçu and Köse<sup>16</sup> similarly observed a reverse relationship between age and the distance from the CS palatal opening to the BCB, showing a significant decrease in distance as age increases. This phenomenon may be due to the significant decrease in alveolar ridge width with increasing age. The exclusion of cases with missing teeth in the observed area enhances the scientific rigor of this study, surpassing Tomrukçu and Köse<sup>16</sup> by eliminating the influence of missing teeth on the alveolar ridge.

# CS Palatal Opening and Gender

Gender-based differences in the distance from the CS palatal opening to BCB and ACR are significant, consistent with the findings of Wanzeler et al<sup>6</sup> and De Oliveira-Neto et al<sup>21</sup>. The distance from the CS palatal opening to BCB and ACR was greater in males compared to females, possibly due to anatomical variations in the shape, size, and bone density of the alveolar ridge, resulting in a higher alveolar ridge in males. Therefore, during anterior teeth implantation surgery in females, careful attention should be paid to measuring the distance from the CS to the buccal bone wall and the top of the alveolar ridge within the alveolar ridge. This is essential for determining the type and size of the implant and ensuring optimal bone integration while minimizing or preventing damage to the CS structure, thus enhancing the success rate of implant surgery. However, Tomrukçu and Köse<sup>16</sup> reported contrasting findings (female>male), possibly due to a higher prevalence of missing teeth in males. Nevertheless, further investigation into the specific reasons is warranted, considering the inclusion of cases involving missing teeth in their study.

# CS palatal opening and long axis of incisal foramen

There is no statistically significant difference in the distance from the CS palatal opening to the NCF and the long axis of the incisal foramen among different genders and age groups. Tomrukçu and Köse<sup>16</sup> study was the only one found on the relationship between CS and the long axis of the incisal foramen. Their study examined the CS structures between the roots of the left and right central incisors, revealing an average distance of 3.66 mm between the CS and the incisal foramen, whereas, in this study, the average distance was 6.210 mm. This difference may be attributed to the larger experimental region in this study compared to Tomrukçu and Köse<sup>16</sup>, which focus on the central incisor area.

# Significance of the Study

Prior to any surgery, clinicians must meticulously analyze the anatomical structure of the operative site and assess its condition to minimize the risk of complications and surgical failure. Prior to carrying out anterior teeth implantation surgery, suitable implants should be selected, and their length and position determined based on the implantation area and anatomical structure<sup>17,24,25</sup>. With the rising number of implant cases in the anterior teeth region, the significance of the CS structure in this area has become increasingly apparent.

Based on the analysis of 159 eligible patients and a comparison with relevant literature, this study concludes that CS is a prevalent anatomical structure irrespective of age and gender. Despite the small diameter of CS in comparison to the conspicuous structure of the incisal foramen, clinicians should not overlook this structure during the surgical procedure. CBCT plays an irreplaceable role in diagnosing and analyzing CS prior to implant surgery. Greater accuracy in CBCT analysis allows for the examination of smaller CS structures, facilitating preoperative assessment of the surgical area and the development of a surgical plan to minimize harm to the CS structure and assess and mitigate surgical risks and complications.

This study examined the presence and positioning of CS (the distance between the palatal opening of CS and BCB, NCF, ACR, and the long axis of the incisal foramen) and its association with gender and age, revealing no significant differences in the presence and positioning of CS across different age groups. Patients from various age groups should be treated equitably, and the analysis of CS should not be disregarded based on assumptions about the likelihood of CS presence in specific age groups. Additionally, this study observed that the distance between CS, BCB, and ACR is shorter in females than in males.

# Shortcomings of Experimental Design

(1) This study systematically excluded cases involving missing teeth in the anterior dental region. In clinical practice, patients undergoing implantation may have experienced tooth loss in the implantation area over time, leading to remodeling of the alveolar ridge and consequent changes in the relative position of the CS structure to the alveolar ridge. (2) As patients age in clinical practice, some individuals in the older age brackets fail to meet the inclusion criteria, leading to a smaller sample size in these groups, thus impacting the accuracy of the findings. (3) The sample size is insufficient to adequately represent the broader Chinese population.

# Conclusions

The CS represents a prevalent anatomical structure. CS has a prevalence rate of 59.75% in the general population, typically exhibiting a curved shape, and is frequently located in the

anterior dental region, particularly in the area of the lateral incisors. Females exhibit a shorter distance between the CS palatal opening position and BCB and ACR compared to males, and this distance decreases with age.

### **Conflict of Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### **Ethics Approval**

This study was approved by the Affiliated Stomatological Hospital of Southwest Medical University (Approval No: 20201210001).

### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

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### Availability of Data and Materials

All data used to support the findings of this study are available from the corresponding author upon request.

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### Authors' Contribution

Conceptualization: W.-X. Rao, L.-Y. Fan; Design: W.-X. Rao, L.-Y. Fan; Data collection: W.-X. Rao, Y.-M. Wen, Y.-X. Ma, Y.-L. Rao, J.-Q. Wu, W.-W. Xiao; Analysis: W.-X. Rao, Y.-X. Ma, M.-X. Li, Y.-M. Wen, Y.-L. Rao, J.-Q. Wu, W.-W. Xiao, L.-Y. Fan; Manuscript preparation: W.-X. Rao; Supervision and Review: L.-Y. Fan, M.-X. Li. All authors gave their approval to submit.

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