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Three-dimensional finite element modeling for evaluation of laryngomalacia severity in infants and children

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Abstract

This study was performed to investigate the feasibility of using a three-dimensional (3D) finite element model for laryngomalacia severity assessment. We analyzed laryngeal computed tomography images of seven children with laryngomalacia using Mimics software. The gray threshold of different tissues was distinguishable, and a 3D visualization model and finite element model were constructed. The laryngeal structure parameters were defined. The peak von Mises stress (PVMS) value was obtained through laryngeal mechanical analysis. The PVMS values of the laryngeal soft tissue and cartilage scaffolds were independently correlated with disease severity. After stress loading the model, the relationship between laryngomalacia severity and the PVMS value was apparent. However, the PVMS value of laryngeal soft tissue was not correlated with laryngomalacia severity. This study established the efficacy of a finite element model to illustrate the morphological features of the laryngeal cavity in infants with laryngomalacia. However, further study is required before widespread application of 3D finite element modeling of laryngomalacia. PVMS values of the laryngeal cartilage scaffold might be useful for assessment of laryngomalacia severity. These findings support the notion that structural abnormalities of the laryngeal cartilage may manifest as quantifiable changes in stress variants of the supraglottic larynx.

Keywords

Pediatric larynx, laryngomalacia, three-dimensional finite element, peak von Mises stress, morphology, cartilage scaffold

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Introduction

Laryngomalacia is characterized by inspiratory laryngeal wheezing and upper respiratory tract obstruction caused by supraglottic tissue prolapse during inhalation. Congenital laryngeal dysplasia is common among newborns and children, accounting for 60% to 70% of newborn laryngeal wheezing.[1] Most children develop symptoms within 2 weeks of birth, with 10% of cases requiring surgical treatment.[2,3]

There are several hypotheses for the etiology of laryngomalacia, including anatomical theory, cartilaginous theory, neural theory, and a combination of the three. Anatomical theory, which is the most widely accepted theory, hypothesizes that abnormal collapse of supraglottic tissue into the laryngeal entrance during inhalation leads to laryngeal wheezing, airway obstruction, and even suffocation. A prospective controlled study showed that the ratio of the arytenoid epiglottic cleft length to the vocal cord length in patients with severe laryngomalacia was significantly different from that in a control population.[4] Anatomical abnormality of the supraglottic tissues may be an important etiological source of laryngomalacia.

Tracheotomy was the only effective treatment for laryngomalacia before the 1980s. In 1984, Lane et al.[5] reported the first case of supraglottoplasty achieved by removing the excess occlusive tissue from the supraglottic posterior portion. The procedure has since been widely used and improved during the past 30 years. Optimization of the location and extent of resection determined by the specific obstruction mechanism of each patient has been particularly notable.[6,7] Although laryngomalacia tends to spontaneously resolve, surgical intervention remains a crucial treatment in patients with a supraglottic anatomical abnormalities. One review of the follow-up results of 89 children with laryngomalacia showed that patients who underwent supraglottoplasty had better outcomes than patients who did not undergo this procedure.[8] Preoperative evaluation of the laryngeal cavity and severity of the laryngomalacia allowed for a personalized surgical plan to achieve balance between respiratory function and swallowing function restoration, both of which are critical components to the success of the operation.

Recent reports have indicated that the three-dimensional (3D) finite element model is of great practical value for the biomechanical study of human tissues.[9,10] Preliminarily, our group used 3D finite element technology to illustrate the structure of the laryngeal cavity of normal children and children with laryngomalacia to assess the different responses of the supraglottic tissues to varying degrees of stress.[11] In the present study, we increased the sample size of the preliminary study to construct a laryngeal cavity model of children with different severities of laryngomalacia. Additionally, these 3D models were used to analyze differences in the response of the supraglottic tissues to varying stressors in the two groups of children, allowing for investigation of the feasibility of the laryngeal cavity model to be used for preoperative evaluation of laryngomalacia severity in the clinical setting.

Materials and methods

Clinical data

Seven children with laryngomalacia who were admitted to the Department of Otolaryngology, Head and Neck Surgery of Shanghai Children's Hospital for supraglottoplasty were recruited. Laryngoscopy (Olympus OTV-S7V Camera System; Olympus, Tokyo, Japan) was performed before the surgery to clarify the diagnosis and simultaneously identify other

Table 1. Patients' demographic and disease characteristics.

Patient No.	Sex	Age	Age at onset	Weight	Height	Comorbidities	Degree of laryngeal obstruction (grade)
1	Female	6 months 18 days	2 months 18 days	4.5 kg	57 cm	Congenital heart disease, growth retardation, pneumonia	II
2	Male	5 months 22 days	4 months	7 kg	60 cm	Pneumonia	II
3	Female	2 months 29 days	1 day	5 kg	52 cm	Pneumonia	I
4	Male	1 month 17 days	10 days	4 kg	50 cm	Growth retardation, pneumonia	I
5	Male	1 month 27 days	7 days	6 kg	58 cm	Pneumonia	I
6	Female	3 months 6 days	7 days	5.8 kg	60 cm	Pneumonia	II
7	Male	5 months 27 days	2 months 27 days	7 kg	64 cm	Pneumonia, tongue root cyst	I

associated diseases of the throat. Children with laryngomalacia required a preoperative 3D computed tomography (CT) examination of the upper respiratory tract, which was performed as a spiral volume scan of the neck (GE LightSpeed VCT; GE Healthcare, Chicago, IL, USA), to comprehensively evaluate the upper respiratory tract and exclude other obstructive diseases of the upper respiratory tract. The neck CT data of the recruited children were used as the experimental materials, and no new examination items or intervention measures were added. The parents of all participants in this study provided written informed consent prior to enrollment. The demographic and disease characteristics of the children are shown in Table 1.

Development of 3D geometric model and finite element model of the laryngeal cavity

In this study, we adopted a method similar to our previous finite element model of the pediatric laryngeal cavity.[11] Materialise Mimics software (Materialise NV, Leuven, Belgium) was used to enhance the DICOM image data obtained by CT scanning. By defining the gray threshold, relevant

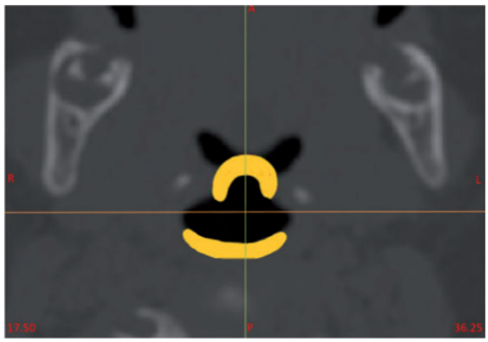

Figure 1. Computed tomography scan of the larynx.

structures of the larynx, including cartilage and soft tissue, were identified and extracted from the CT data as shown in Figure 1. Smoothing parameters were set to remove redundant data, and a 3D model reflecting the geometry of the laryngeal cartilage and soft tissue in infantile laryngomalacia was finally established, including the laryngeal cartilage scaffolds and the soft tissue structure attached to the cartilage scaffolds (Figure 2).

Finite element analysis of the model

The ultimate purpose of a finite element analysis model is to analyze the differences

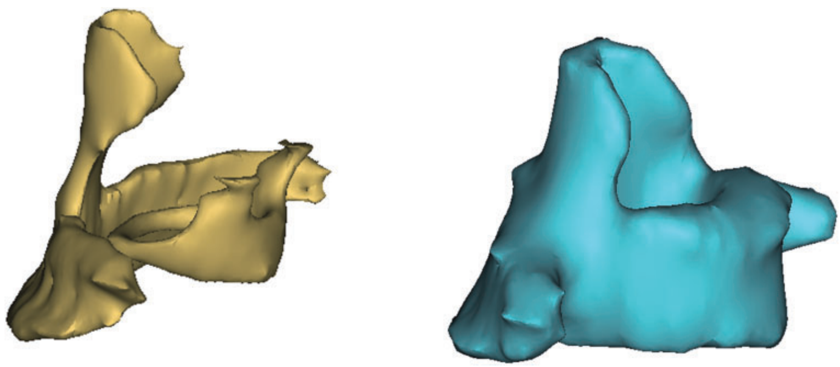

Figure 2. Geometric model of the laryngeal cartilage and soft tissue.

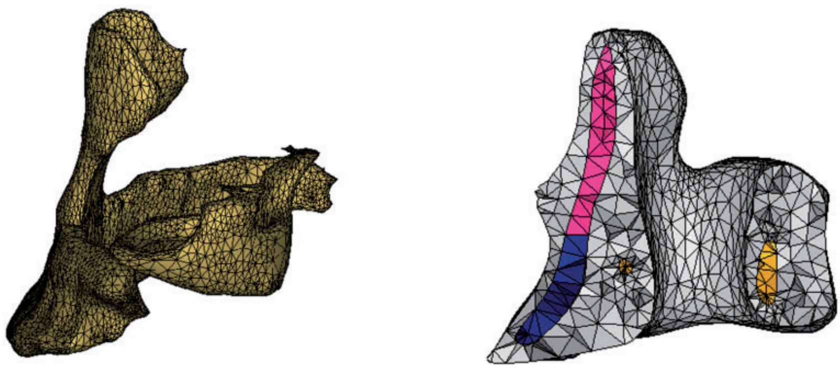

Figure 3. Finite element model of the laryngeal cartilage and soft tissue.

in the response of supraglottic tissue to stress among the laryngeal cavities of children with varying degrees of congenital laryngomalacia. These analytical methods are specifically described later in the Materials and methods section. Briefly, stress on the glottis tissues is simulated in the model as the force of airflow. Finite element mesh division is achieved via HyperMesh software (Altair Engineering Inc., Troy, MI, USA) before biomechanical analysis of the laryngeal cavity model of children with laryngomalacia. In this study, tetrahedral mesh was specifically used to divide the overall laryngeal cavity structure, and the finite element model of the laryngomalacia cavity was finally obtained as shown in Figure 3.

Material setting

The physiological structure of laryngeal cartilage and soft tissue is superficially complex. Further, its mechanical properties are characterized by nonlinearity, anisotropy, and heterogeneity. To simplify the calculation process, the material properties of the model were simplified to some extent in the mechanical analysis. The laryngeal cartilage strut and soft tissue structure were respectively set as isotropic, homogeneous, and continuous linear elastic materials. According to previous reports,[12,13] the estimated elastic modulus and Poisson's ratio of the laryngeal cartilage scaffold are 60 MPa and 0.47, respectively. The estimated elastic modulus and Poisson's ratio of the soft tissue layer are 13 MPa and 0.49, respectively.

Measurement of von Mises stress after stress loading to the model

The positive end-expiratory pressure of the ventilator reflects the stress of airflow on the laryngeal cavity to some extent. Normal neonatal positive end-expiratory pressure is reportedly set at 3 to 8 cm H_2O,[14] where the median value of 5 cm H_2O was taken as the pressure value and applied uniformly as the pressure perpendicular to the external surface of the larynx in a previous laryngomalacia model. From the seven collective laryngomalacia models, a von Mises stress cloud diagram was constructed using the post-processing function of Abaqus software (Abaqus Inc., Palo Alto, CA, USA). The peak stress of the laryngeal soft tissue and laryngeal cartilage scaffold were measured simultaneously.

Assessment of severity of laryngomalacia in children

No uniform standard for scoring the severity of infantile or pediatric laryngomalacia has yet been established. In our previous report, both symptomatic and clinical scores were developed and initially confirmed in the assessment of the severity of laryngomalacia.[15]

Symptom scores were measured on a visual analog scale that included wheezing, regurgitation or feeding difficulty, choking, dyspnea, and the frequency or severity of pneumonia. The visual analog scale score, which was assessed by the patients' parents according to subjective symptoms, ranged from 0 (least severe) to 10 (most severe) for five items, and the highest total possible score was 50.

The clinical score was assessed by the physician according to the degree of laryngeal obstruction: no obstruction, 0; grade I obstruction, 1 to 3; grade II obstruction, 4 to 7; and grade III obstruction, 8 to 10. The morphology of the glottis under laryngoscopic examination was also assessed: normal morphology, 0; laryngomalacia with clear visualization of the vocal cords in the inhalation phase and exhalation phase, 1 to 3; laryngomalacia with clear visualization of the vocal cords only in the exhalation phase, 4 to 7; and laryngomalacia with no visualization of the vocal cords in either the exhalation phase or inhalation phase, 8 to 10. Swallowing function was scored as follows: no secretion in the throat, 0; small amount of secretion in the throat, 1 to 3; large amount of secretion in the throat and piriform fossa, 4 to 7; and piriform fossa filled with effusion, 8 to 10. Weight was scored as follows: normal, 0; lower than normal within 10%, 1 to 3; lower than normal within 20%, 4 to 7; and lower than normal more than 20%, 8 to 10. Polysomnography was graded as follows: minimum oxygen saturation of 93% to 100%, 0; 85% to 92%, 1 to 3; 75% to 84%, 4 to 7; and $\leq$74%, 8 to 10. If no polysomnography data were available, the oxygen saturation under electrocardiographic monitoring was scored as follows: 97% to 100%, 0; 90% to 97%, 1 to 3; 80% to 90%, 4 to 7; and $<$80%, 8 to 10. The highest possible clinical score was 50 points based on each parameter collectively. The maximum symptom score and clinical score combined was 100 points.

Correlation analysis of von Mises stress and severity score in pediatric laryngomalacia model

SigmaPlot 12 software (Systat Software Inc., San Jose, CA, USA) was used for the statistical analysis. Spearman correlation was then used to analyze the correlation between the severity of laryngomalacia and the peak von Mises stress of the laryngeal soft tissue and laryngeal cartilage scaffold. A P value of <0.05 was defined as statistically significant.

Results

Three-dimensional finite element model of pediatric laryngomalacia

Materialise Mimics software was used to process the DICOM image data obtained through CT scanning to construct the 3D geometric model of the laryngeal cavity, as shown in Figure 4. Ultimately, the software built the finite element models as shown in Figure 5 (Patients 1 and 7). The 3D geometric model of the laryngeal bone structure and soft tissue was extraordinarily vivid, with no distortion, jagged edges, or simplification on the surface of the model. Based on the geometric model, the finite element model achieved a reasonable amount of mesh division. The mesh was dense in places with large curvature variation or small structures and sparse in places with large areas and smooth curvature, effectively reducing the number of grids to be analyzed (more cost-effective).

Comparison of von Mises tension after loading stress in models with different degrees of pediatric laryngomalacia

As observed in the von Mises stress cloud diagram, the tension distribution was relatively homogeneous in the models of the seven children, with the main tension concentrated in the supraglottic region. The peak von Mises stress of the laryngeal soft tissue and laryngeal cartilage scaffold in the seven patient models is shown in Table 2. After the stress was applied, the peak von Mises stress values of the seven cases of laryngomalacia (of varying severity) were significantly different. The largest peak von Mises stress of laryngeal soft tissue was observed in Patient 1 (0.289 MPa), and the smallest peak was observed in Patient 4 (0.068 MPa). The largest peak von Mises stress of the laryngeal cartilage scaffold was similarly observed in Patient 1 (0.27 MPa) and the smallest in Patient 7 (0.069 MPa).

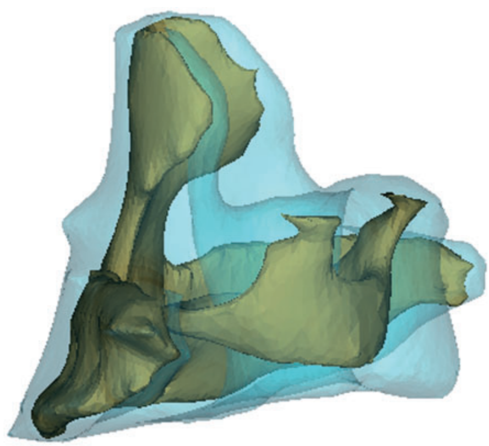

Figure 4. DICOM images obtained by Materialise Mimics software through computed tomography scanning.

Score of severity of laryngomalacia in children

The severity scores of laryngomalacia were significantly different among the seven children, with the lowest score being 14 points and the highest score being 39 points. The specific scores of the seven participating children with laryngomalacia are shown in Table 3.

Correlation analysis results of laryngomalacia stress peak and severity score

Spearman correlation analysis was conducted to evaluate the correlation between the severity score of laryngomalacia and peak von Mises stress of the laryngeal

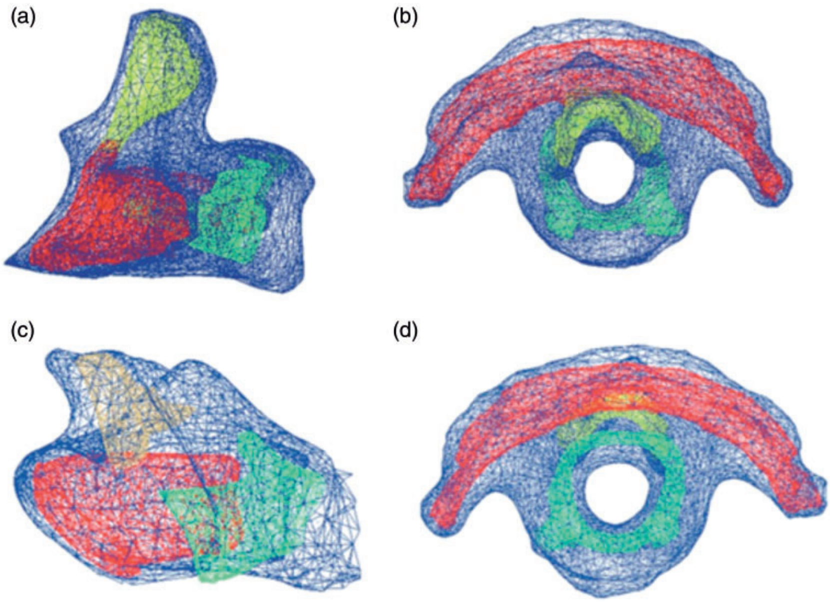

Figure 5. Three-dimensional (3D) finite element model of laryngeal cavity in children with larynomalacia. (a) Left-side view of 3D model in Patient 7. (b) View from above on 3D model in Patient 7. (c) Left-side view of 3D model in Patient 1. (d) View from above on 3D model in Patient 1.

Table 2. Peak stress of laryngeal soft tissue and laryngeal cartilage scaffold in children with varying degrees of laryngomalacia.

Patient No.	1	2	3	4	5	6	7
Peak von Mises stress of laryngeal soft tissue (MPa)	0.289	0.124	0.152	0.068	0.092	0.127	0.242
Peak von Mises stress of laryngeal cartilage scaffold (MPa)	0.27	0.156	0.086	0.101	0.138	0.176	0.069

Table 3. Severity scores of laryngomalacia in the seven children.

Patient No.	1	2	3	4	5	6	7
Total score	39	34	22	29	33	36	14

cartilage scaffold. The correlation coefficient was 1 and the P value was <0.001, indicating a statistically significant positive correlation between the two factors. The severity score of laryngomalacia and the peak von Mises stress of the laryngeal cartilage scaffold tended to increase simultaneously. However, Spearman correlation analysis showed no correlation between the peak von Mises stress of the laryngeal soft tissue and the severity score of laryngomalacia.

Discussion

Application prospectus of a finite element laryngomalacia model

The most common cause of neonatal laryngeal wheezing is laryngomalacia.[16] Anatomical abnormality of the suprasegmental tissue is an important factor in the occurrence and development of laryngomalacia.[4] Electronic laryngoscopy is an important tool for the diagnosis and classification of congenital laryngomalacia; however, quantitative evaluation of the disease severity is difficult. For severely affected children, 3D CT of the upper airway is also an important examination method. However, 3D CT of the airway can only illustrate the structural characteristics of the laryngeal cavity of children; it cannot determine the actual deformation of the supraventricular tissue when airflow passes through. In contrast, a 3D finite element model can be used for diagnosis and evaluation of the severity of laryngomalacia from both structural and functional aspects.

With the application of plasma technology to supraglottoplasty, increasingly more children with relatively mild laryngomalacia have benefited from surgical intervention. The application of plasma technology to supraglottoplasty was investigated in our earlier work.[17] Swallowing function is a more important indicator of the success or failure of laryngomalacia surgery than is respiratory function. Nevertheless, postoperative respiratory function and swallowing capacity are often contradictory. Excessive opening of the glottis and lifting of the epiglottis may cause postoperative choking, coughing, or aspiration. Along with the improvement of the finite element model of laryngomalacia and the improved visualization of the postoperative laryngeal cavity during a stress state, the model can be used to design personalized surgical plans and preoperatively estimate the postoperative laryngeal structure, respiratory function, and swallowing function according to the different estimated surgical resections. This facilitates an improved balance between the recuperation of respiratory and swallowing functions.

Characteristics of a finite element model of a pathological laryngeal cavity in infants

The accuracy of finite element modeling to calculate the stress on the glottis depends on the accuracy of the original geometric model. In our previous work, we used CT data obtained from the laryngeal cavity of three children to preliminarily establish a limited finite element model of a pediatric laryngeal cavity.[11] However, after the application of this technology to young infants, we found that the resolution of the CT data of the children was lost after amplification because of the small volume of the laryngeal cavity. It was thus difficult to automatically identify the laryngeal cavity structure using Materialise Mimics software. Therefore, in the present study, we redefined the gray threshold and subdivided it to enable automatic recognition. The smoothing procedure of CAD software was improved to obtain a geometric model more consistent with the 3D structure of the infant laryngeal cavity.

The CT data were obtained with the GE LightSpeed VCT high-resolution CT scanner. The scanning speed was 88 mm/s. The laryngeal cavity height of the seven children with laryngomalacia was <2 cm as calculated using the 3D model. The time required for a CT scan of the whole of laryngeal cavity was <250 ms. When sleeping, the newborn respiratory rate is normally 40 bpm. The duration of each breathing cycle was >1500 ms. Therefore, a CT scan of the upper respiratory tract can go through the entire laryngeal cavity of the patient in a single inhalation phase or exhalation phase without artifacts caused by respiratory movement. Further, use of CT equipment with higher scanning efficiency can more effectively avoid artifacts.

In this study, the geometric parameters of the laryngeal cavity of infants and young children were extracted directly from 3D

CT images, which reflected the actual structure of the laryngeal cavity of children with laryngomalacia to the greatest extent and ensured the accuracy of the geometric model construction. The finite element model could thus reliably illustrate the pathological state of laryngomalacia more accurately.

Application of a laryngomalacia finite element model for evaluation of disease severity

In this study, we measured von Mises stress to analyze the biomechanical results of the study; this technique has been applied in many previous studies.[18] Previous studies have also been conducted to preliminarily discuss the value of 3D finite element modeling of the laryngeal cavity and the results of biomechanical analysis in clinical application.[11,19] Briefly, investigators constructed a 3D finite element model of two children with laryngomalacia and one normal child and determined the von Mises stress. The results showed that the peak von Mises stress values of the two children with laryngomalacia were higher than that of the normal child. Similarly, the peak von Mises stress value of the children with more severe clinical symptoms was higher than that of the children with less severe clinical symptoms, suggesting that the von Mises stress reflects the biomechanical state of the laryngeal cavity. Comparison of Tables 2 and 3, which show the disease severity scores of children with laryngomalacia, indicates that the peak von Mises stress capacity of the laryngeal cartilage scaffold followed a similar trend. For example, Patient 1 was the most severe, with severe pneumonia and growth retardation before surgery and grade II preoperative laryngeal obstruction. Only one of the other patients was affected by pneumonia and growth retardation in conjunction with grade I laryngeal obstruction. The remaining five patients were affected by either pneumonia or growth retardation independently. Thus, Patient 1 showed the highest severity score and the highest peak von Mises stress value of the laryngeal cartilage scaffold (39 and 0.27 MPa, respectively).

As seen from the clinical data, all seven children presented with pneumonia. Among them, four patients presented with pneumonia, growth retardation or pneumonia, and grade II laryngeal obstruction. Only three patients (Patients 3, 5, and 7) presented with pneumonia along with grade I laryngeal obstruction. The disease severity of these three children was mild, and the peak von Mises stress of their corresponding laryngeal cartilage scaffolds was also low. Apart from laryngomalacia, another important surgical indication in Patient 7 was the observation of a tongue root cyst that blocked the airway and affected the patient's ventilation. Therefore, in comparison, the laryngomalacia was least severe in Patient 7 (score of 14). Similarly, the peak von Mises stress value of the laryngeal cartilage scaffold was lowest in Patient 7 (0.069 MPa).

Spearman correlation analysis was conducted to analyze the relationship between the severity score of laryngomalacia and the peak von Mises stress value of the laryngeal cartilage scaffold using SigmaPlot 12 software. The result was statistically significant and the two parameters were positively correlated, suggesting that the change in stress on the laryngeal supraglottic region might be related to structural abnormalities of the laryngeal cartilage. There was no significant correlation between the severity score of laryngomalacia and the peak von Mises stress value of the laryngeal soft tissue in all seven children.

The severity score in Patients 1, 2, 5, and 6 was >30, and the peak von Mises stress value of the laryngeal soft tissue was 0.289, 0.124, 0.092, and 0.127 MPa, respectively.

In the other two remaining patients, the von Mises stress of the laryngeal soft tissue exceeded 0.092 MPa while the severity score of laryngomalacia was <30. The severity score in Patient 7 was the lowest at 14, but the peak von Mises stress in the laryngeal soft tissue was as high as 0.242 MPa. Combined with the statistical results obtained from SigmaPlot 12 software, the Spearman correlation analysis showed no correlation between the peak von Mises stress value of the laryngeal soft tissue and the severity score. This finding suggests that the change in stress in the laryngeal supraglottic region has no relationship with structural abnormalities of the laryngeal soft tissue.

Therefore, we conclude that the peak von Mises stress value in a 3D finite element model of laryngomalacia can reflect the severity of laryngomalacia to some extent and that the change in stress in the laryngeal supraglottic region might be related to structural abnormalities of the laryngeal cartilage. In this study, the parameters of the cartilage and soft tissue used to construct the model were derived from the existing literature.[12,13] The specific parameters were mentioned in the subsection titled "Material setting" earlier in the manuscript. The peak von Mises stress value is mainly affected by the geometry of the model; therefore, although most of these parameters were derived from adult data rather than pediatric data, we predicted that this would not have a significant effect on the results of pediatric patients. However, in future work, children's laryngeal parameters can be obtained by tissue sample measurement to improve the accuracy. Moreover, further investigation in a larger sample is needed to validate the results of the von Mises stress analysis and clinical data obtained in the present study.

In conclusion, a 3D finite element model of laryngomalacia was developed with spiral CT images by means of Mimics and Abaqus software. The 3D model of the laryngeal cartilage scaffold and soft tissue may contribute to further biomechanical studies, postoperative outcome prediction strategies, and surgical approach designs. The peak von Mises stress value, especially that of the laryngeal cartilage structure, might be used to quantitatively assess the severity of laryngomalacia in infants and children.

Highlights

- A 3D finite element model of laryngomalacia can reflect laryngomalacia severity.
- Laryngeal supraglottic stress may indicate laryngeal cartilage abnormalities.
- Laryngeal supraglottic stress does not reflect laryngeal soft tissue abnormalities.
- Peak von Mises stress may be used to quantitatively assess pediatric laryngomalacia severity.

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Authors' contributions

Hongming Xu and Xiaoyan Li participated in the study design and data collection. Jiali Chen participated in the data analysis, statistical analysis, manuscript preparation, and data interpretation. Shilei Pu was involved in the data collection and patient test procedures.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Institutional review board statement

This research did not increase the patients' risk or economic burden, the patients' rights were fully protected, and the project design was conducted in line with scientific and ethical principles. The institutional review board approved this project.

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