Correlation between clinical risk factors and tracheal intubation difficulty in infants with Pierre-Robin syndrome: A systematic review

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Research article

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Abstract

Background: Difficult tracheal intubation is a problem commonly encountered by anesthesiologists in the clinic.

Methods: In this retrospective study, case-level clinical data and computed tomography images of 96 infants with Pierre-Robin syndrome were included in the analysis. First, computed tomography images were labeled by a clinically experienced physician. Then color space conversion, binarization, contour acquisition, and area calculation processing were performed on the annotated files. Finally, we calculated the correlation coefficient between the seven clinical factors and tracheal intubation difficulty, and the difference in each risk factor under tracheal intubation difficulty.

Results: The absolute value of the correlation coefficient between throat area and tracheal intubation difficulty is 0.54, and the difference of throat area under tracheal intubation difficulty is significant. Body surface area, weight and gender also show significant difference under tracheal intubation difficulty.

Conclusions: There is a significant correlation between throat area and tracheal intubation difficulty in infants with Pierre-Robin syndrome. Body surface area, weight and gender may have an impact on tracheal intubation difficulty in infants with Pierre-Robin syndrome.

Background

Difficult tracheal intubation is common in clinical practice, mostly referring to tracheal intubation that cannot be successfully completed by ordinary indirect laryngoscope [1]. It is the most difficult problem encountered by anesthesiologists in their daily work, mainly caused by anatomical deformities, restricted back tilting activities, obesity and limited mouth opening [2]. These factors have an adverse effect on treatment effect. In practice, before formal implementation of tracheal intubation, the level of difficulty is first evaluated. For patients with different levels of difficulty, preparations should be done in advance to avoid local mucosal damage caused by multiple intubation or complications such as dislocation of the circular cartilage [3].

In 2016, Münster et al. [4] reported that the position of vocal cords was related with laryngeal exposure, and that difficult laryngoscopy was more likely when vocal cords were closer to the head. From 2016 to 2017, many studies have utilized ultrasound for the clinical diagnosis of difficult tracheal intubation [5][6][7][8][9]. Ultrasound not only provides real-time images, but also reveals dynamic structural changes of the airway. In 2019, Lee et al. [10] found that the distance from mandibular groove to hyoid bone and the distance from the inner edge of mandible to hyoid bone on X-ray images of the lateral neck were important for predicting difficult tracheal intubation in patients with acromegaly. However, few methods exist for infant airway assessment and the accuracy is relatively poor.

Pierre Robin syndrome (PRS) [11] is the triad of micrognathia, glossoptosis, and cleft palate. These conditions could easily lead to difficult tracheal intubation which is the greatest risk factor for intubation anesthesia. Accurate preoperative prediction of intubation difficulty and adequate preparations are key to ensuring successful airway management in infants with PRS. There have been many methods for assessing the difficulty of tracheal intubation [12], but no suitable method exists for infants, especially infants with PRS. Moreover, few reports have focused on the application of computed tomography (CT) on tracheal intubation difficulty assessment in infants with PRS [13]. Therefore, this study was conducted to assess the difficulty of tracheal intubation in infants with PRS by incorporating CT to guide airway management for anesthesia.

Methods

Dataset

The study collected clinical information and CT images from infants with PRS undergoing intubation anesthesia in 2018 from Children's Hospital of Nanjing Medical University. This retrospective study was approved by local institutional review board and waived the requirement for informed consent based on minimal harm to the patient.

Seven clinical risk factors [14] that may have an impact on tracheal intubation difficulty were provided by experienced clinicians, including gender, height, weight, body surface area (BSA), throat area, age, and pneumonia (Table 1). The calculation of throat area will be elaborated below, and the remaining indicators can be directly obtained or simply calculated. Tracheal intubation difficulty is divided into three levels based on whether glottis can be completely observed under visual laryngoscope, of which level □ refers to complete observation, level □ refers to partial observation, and level □ refers to the case when only epiglottis can be observed.

Table 1

Clinical information for children with PRS.

Gender	Male: Female	48: 48
Height (Unit: m)	Median (1st Qu., 3rd Qu)	0.5000 (0.5000, 0.5300)
Weight (Unit: kg)	Median (1st Qu., 3rd Qu)	3.400 (3.000, 3.800)
BSA (Unit: m^2)	Median (1st Qu., 3rd Qu)	0.2190 (0.2050, 0.2330)
Throat area (Unit: pixel)	Median (1st Qu., 3rd Qu)	1440.5 (1237.2, 2034.4)
Age (Unit: day)	Median (1st Qu., 3rd Qu)	33.00 (13.67, 50.00)
Pneumonia	Yes: No	32: 64

Descriptive statistics of the seven clinical risk factors for 96 infants enrolled in the study. For categorical variables, the frequency of each category is listed. For numerical variables, the first quartile, median and third quartile are calculated.

Labeling criteria

To assess the impact of throat area on tracheal intubation difficulty, the collected CT images (Fig. 1.a) were labeled according to the irregularity of the area being labeled using Labelme, an annotation tool which is based on the Python language and allows for irregular area annotation [15]. A radiologist, who has 20 years of clinical experience and is invisible to the infants' difficulty level for this study, is responsible for labeling. Through three-dimensional reconstruction technique, the median sagittal image of the upper airway of the infants was obtained, and then the area of the oropharyngeal cavity (ie, the pharyngeal area between the plane of the tongue and the glottis) was labeled.

Annotation file processing and area calculation

The overall workflow is shown in Fig. 2. The annotation file generated by Labelme is in the format of .json (Fig. 1.b) [16]. To calculate throat area, the annotation file is first converted to a single-channel image in .png format (Fig. 1.c).

Subsequent processing is performed by OpenCV in the Python environment. First, the single-channel image obtained in the previous step undergoes color space conversion using the cvtColor function of OpenCV and is converted into a grayscale image (Fig. 1.d) [17][19]. The grayscale image is then thresholded (the threshold is set to 1)

using the threshold function and becomes a binary image (Fig. 1.e) [18][19]. The throat contour information of the marker is then obtained by the findContours function, with pixel position difference between two adjacent points in all contour points no larger than 1 [19][20]. Finally, the contour information obtained in the previous step in the form of a point set is input into the contourArea function of OpenCV to calculate the area [19][21].

Correlation analysis

Correlation coefficients computed from correlation analysis were used to assess the impact of each risk factor on tracheal intubation difficulty. Clinical risk factors highly correlated with difficulty level have better predicative effects in the clinic, and such findings may support subsequent studies.

Statistical analysis

Since clinical risk factors include numerical and categorical variables and tracheal intubation difficulty is categorical, correlation was measured by the Spearman rank correlation coefficient. In addition, to analyze whether there is a significant difference in each clinical risk factor under tracheal intubation difficulty, the Kruskal-Wallis test was performed for numerical factors, and Pearson's Chi-squared test was performed for categorical factors.

Results

The flow chart of the study is shown in Figure 2. Eight infants were excluded due to censored data (4 cases of censored pneumonia data and 4 cases of censored throat area data). Finally, 96 infants were included in the study of which 29 were level □difficulty, 43 were level □ difficulty,

and 24 were level □ difficulty of tracheal intubation. Additional data with sufficient clinical information for the study was collected.

The correlation coefficients are integrated in Figure 3, where darker color indicates stronger correlations, while lighter color represents weaker correlations. The correlation between throat area and tracheal intubation difficulty was the greatest, and the correlation coefficient is -0.54. Risk factors of moderate correlation with tracheal intubation difficulty were BSA, weight and gender, with correlation coefficients of -0.29, -0.29 and 0.26, respectively. All numerical risk factors were negatively correlated with tracheal intubation difficulty. Among categorical risk factors, males were more difficult to intubate than females, and infants with pneumonia had a lower level of difficulty in intubation than infants without pneumonia.

Results of internal difference analysis in risk factors are shown in Table 2. The difference in throat area under tracheal intubation difficulty was significant, with $P < 0.0001$ (Level □ vs. □: $P = 0.0022$, Level □ vs. □: $P = 0.0002$, Level □ vs.□: $P < 0.0001$). The differences in BSA, weight and gender under tracheal intubation difficulty were also significant, and corresponding P values are 0.0117, 0.0117 and 0.0043, respectively. BSA, weight, and gender were significantly different when comparing level □ to level □ and level □ to level □. Height, age, and pneumonia showed no significant difference under tracheal intubation difficulty.

Table 2. Difference analysis results of various factors.

	Level 1 vs. 2	Level 2 vs. 3	Level 1 vs. 3	Total
Gender	1	0.0042 **	0.0125 *	0.0043**
Height	0.2473	0.4621	0.0526	0.1772
Weight	0.476	0.0264*	0.0025**	0.0117*
BSA	0.476	0.0264*	0.0025**	0.0117*
Throat area	0.0022**	0.0002 ***	<0.0001***	<0.0001***
Age	0.4694	0.2924	0.0503	0.1949
Pneumonia	0.4703	1	0.5253	0.5438

P value of each risk factor under tracheal intubation difficulty. Among them, P value of numerical variable is calculated by the Kruskal-Wallis test, and that of categorical variable is calculated by Pearson's Chi-squared test.

* P<0.05
** P<0.01
*** P<0.001

Discussion

In this study, we used clinical data from 96 PRS infants who underwent intubation anesthesia for correlation analysis which demonstrated that throat area had significant effect on tracheal intubation difficulty. The larger the throat area, the lower the level of tracheal intubation difficulty, which is consistent with clinician's subjective perception. In addition, we found that high BSA and weight corresponded to low tracheal intubation difficulty, which may be due to better physical development of such infants. Moreover, male infants had a higher tracheal intubation difficulty than females. Pneumonia, age, and height indicated low correlation with the difficulty of tracheal intubation, which may be related to the small amount of data collected and is worthy of further analysis.

After further P-value analysis, we found that four factors, namely throat area, gender, weight and BSA, were internally different under difficulty of tracheal intubation. Among them, the difference in throat area was significant between all levels of tracheal intubation difficulty. Gender, weight, and BSA were only significantly different between level and level , level and level . We speculate that it may be because the sample size of level tracheal intubation difficulty is too small. In addition, there were no statistically significance in height, age, pneumonia under tracheal intubation difficulty, which may be related to the small sample size, or because there is in fact no statistical significance.

Attention should be paid to some of the limitations of our research. First, we studied the correlation between risk factors and tracheal intubation difficulty without building a predictive model, because the limited number of cases obtained in this study could not meet the requirements for modelling. Secondly, in order to facilitate the drawing of the correlation coefficient map, the correlation measure was based on the Spearman rank correlation coefficient. In addition, the data for this study is single-centered. Finally, the annotation of the region of interest in the throat is done by one experienced doctor, which may be subjectively biased.

Based on the above limitations, following studies can be carried out in the future. First, further study may expand the number of cases collected and construct a predictive model of intubation difficulty. Secondly, regional annotation can be performed by multiple physicians, and artificial intelligence annotation tools can be constructed. Finally, the integration of labeling and difficulty prediction can be realized.

Conclusion

In summary, our study verifies that throat area does have an impact on difficulty level of tracheal intubation in infants with PRS. In addition, gender, weight and BSA may have an effect on intubation difficulty.

Abbreviations

PRS
Pierre Robin Syndrome
CT
Computed Tomography
BSA
Body Surface Area

Declarations

Ethics approval and consent to participate

The local institutional review committee (Nanjing, China) ethically approved the study. The committee waived the requirement for written informed consent.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YIL is the main contributor in writing the manuscript. SZ is responsible for the collection and annotation of CT images. JSW processes the image and calculates the area, and performs statistical analysis. All authors read and approved the final manuscript.

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Not applicable

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Figures

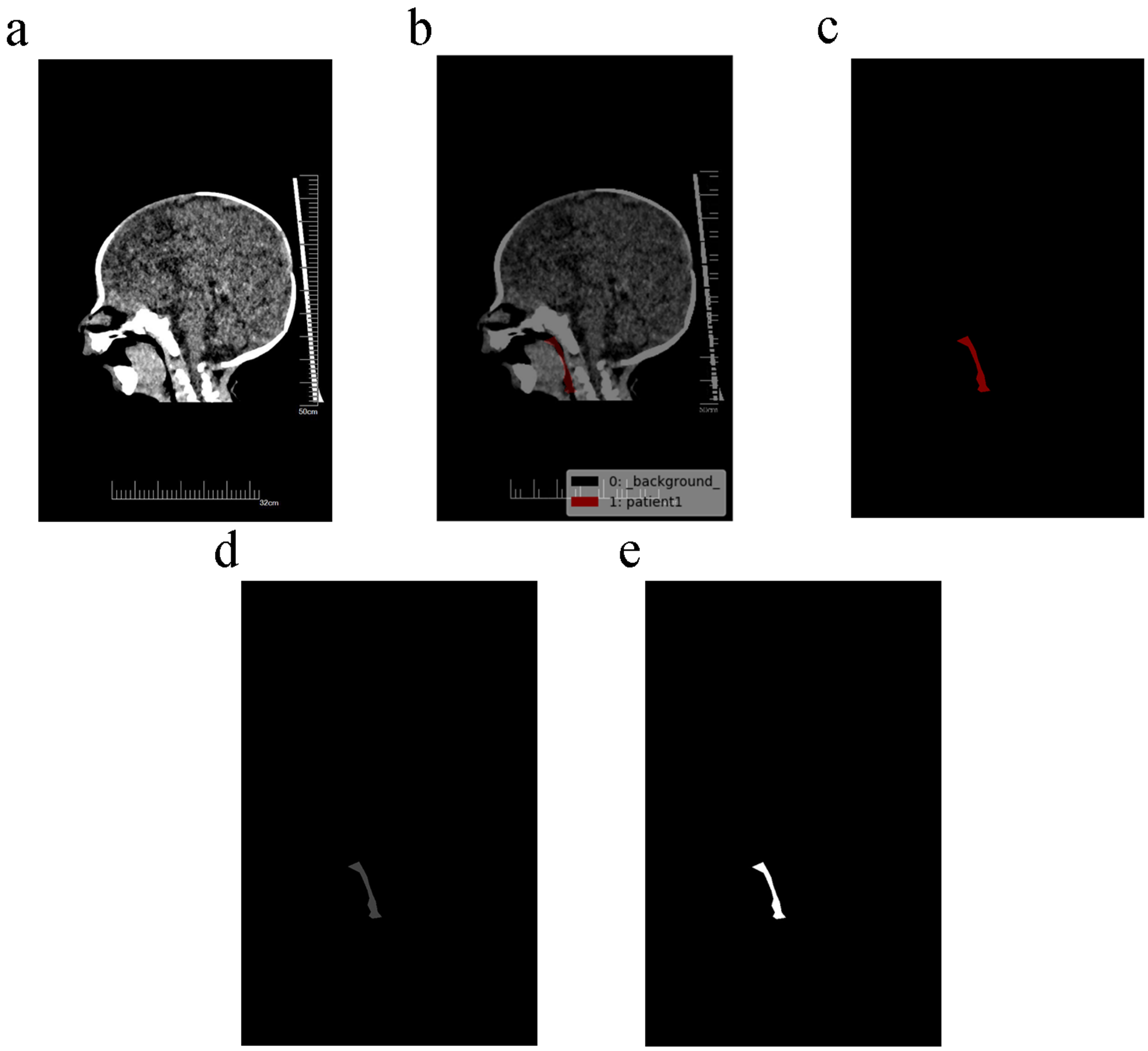

Figure 1

Images generated during area calculation. a. Original CT image. b. The image after labeling by labelme. c. The .png image obtained by single channel conversion. d. The grayscale image obtained by color space conversion. e. The binary image obtained after thresholding is performed.

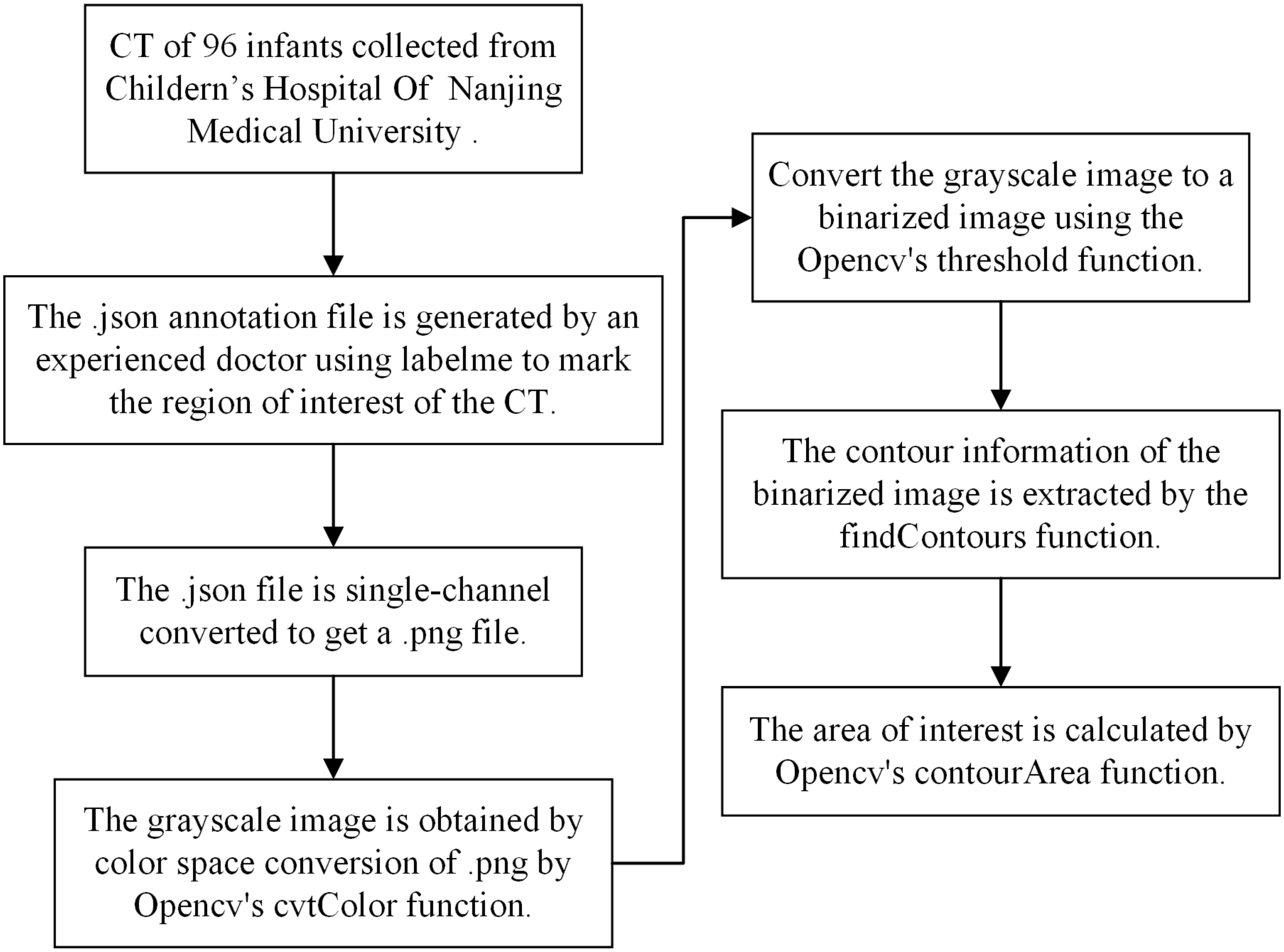

Figure 2

The flow chart for area calculation. The original image was processed by OpenCV for channel conversion, color space transformation, binarization, contour extraction and area calculation.

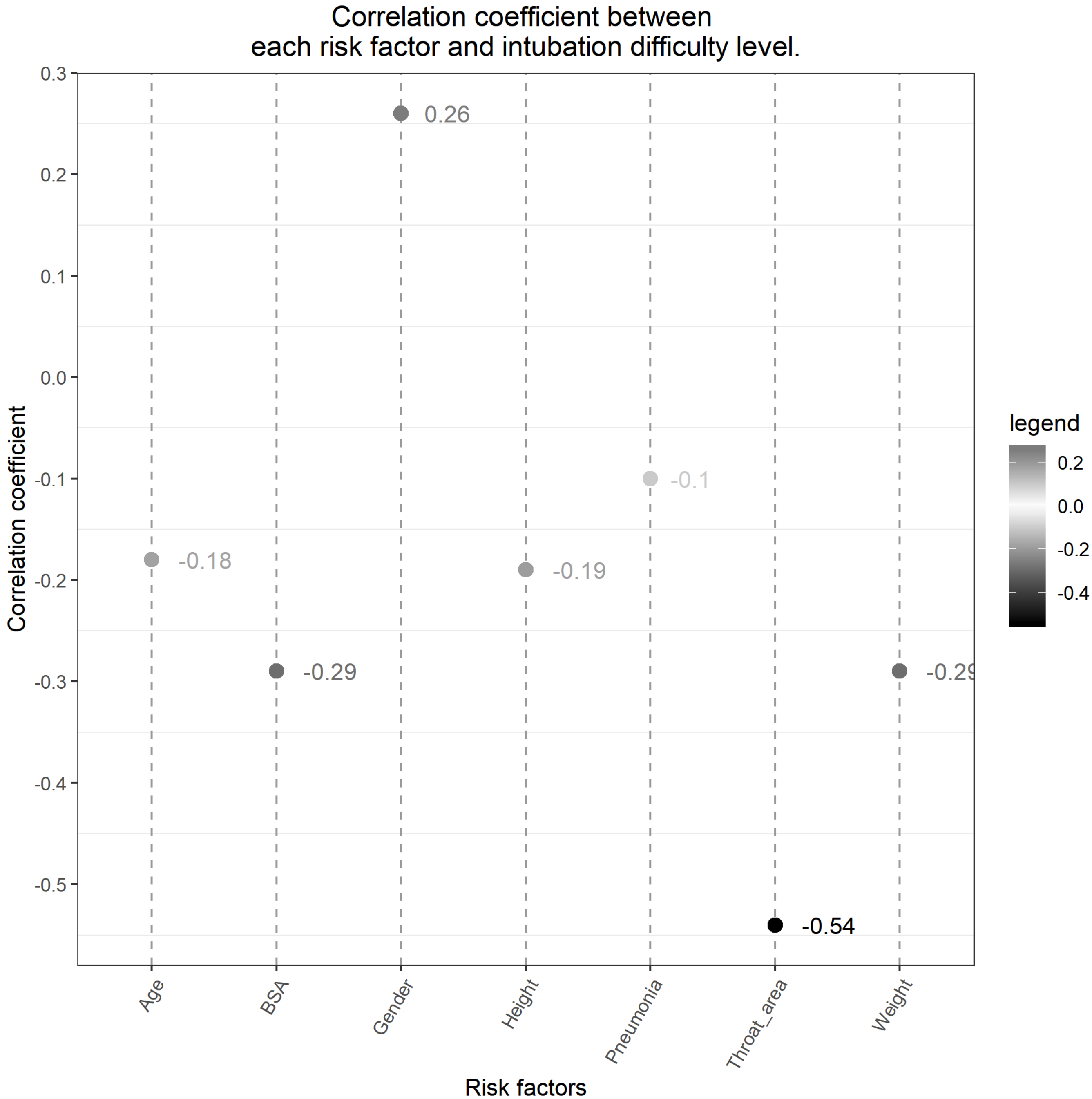

Figure 3

Correlation coefficient graph. The correlation between clinical risk factors and intubation difficulty level, denoted by the Spearman rank correlation coefficient.