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Research article

Long term results in children underwent nuss procedure preschool with pectus excavatum: Real-world study with propensity matching

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ABSTRACT

Background: It is controversial when surgery should be performed for pectus excavatum (PE). The study retrospectively compared the long-term prognosis in PE children undergoing the Nuss procedure at the age of 4–6 versus those performing surgery at the age of 12–14.

Methods: 178 patients were included in the retrospective real-world research. Clinical Characteristics were collected at baseline. The endpoint of the study was set as the last follow-up at the age of 18 in outpatient services. Satisfaction and complication rate were set as the primary outcome and were collected at the endpoint. Hospital stay post-surgery and analgesia dosage were regard as the secondary outcome. To reduce potential bias between two different age groups, propensity score matching (PSM) analysis was analyzed.

Results: The oral analgesic dosage of children in the 4–6 years old age group is significantly lower than that of the 12–14 years old group (0.70/kg, 0.30–1.50/kg versus 1.50/kg, 0.90–2.30/kg, $P < 0.001$), and children in the younger age group are discharged earlier. There was no difference in overall satisfaction (89.1 %, versus 88.20 %, $P = 0.99$) and recurrence rate (7.2 %, versus 6.8 %, $P = 0.99$) between the two groups of when they reach the age of 18.

Conclusions: Performing Nuss procedure at the age of 4–6 does not affect the overall long-term satisfaction of the child or increase the long-term recurrence rate. Surgical intervention in children with pectus excavatum preschool can provide a better postoperative experience in hospital compared with intervention in adolescent.

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1. Introduction

The most common deformity of the chest wall in children is pectus excavatum and most patients are suitable for intervention with Nuss procedure [1]. Currently, Nuss surgery is still controversial in terms of the optimal surgery age [2]. For standard cases, surgeons generally agree that children under 12 should not be corrected for pectus excavatum [3]. The main concern is that early age surgery may increase the risk of perioperative complications and the long-term recurrence rate [4,5].

However, our previous studies have confirmed the safety of early age surgery [6] and found that early age surgery is more beneficial for the psychological development [7] as well as academic performance of children [8]. Meanwhile, according to the experience of Nuss and we center over the past twenty years it seems that early age surgery does not increase the long-term recurrence rate of children if the duration of bar placement is sufficient [9,10].

To confirm this hypothesis that early age surgery does not increase the long-term recurrence and better determine the optimal surgical intervention age for pectus excavatum, we conducted this retrospective cohort study with longest follow-up time of 14 years. The patients were divided into 4–6 years old group and 12–14 years old group. The endpoint was set as the patient reaching the age of 18 and propensity matching score (PSM) will be used to reduce inter group bias.

2. Methods

2.1. Study design and participants

This study was approved by the Ethics Committee of our hospital (approval number: 2021–42). Human participants involving in this study were protected according to the Helsinki Declaration [11], and each child's guardian signed an written authorization. STROCSS [12]and STROBE [13] criteria were applied to report this research.

We collected retrospective data from Clinical Data Center in we hospital from January 2005 to January 2010. Two independent groups extracted and integrated the data, and the third will evaluate inconsistent data and submit it for discussion to all authors.

Visual evaluation and CT scans were used to diagnose pectus excavatum. A number of demographic and baseline characteristics were collected, including patient gender, Haller index (HI), pulmonary function, echocardiography (UCG) and electrocardiogram (ECG). At least two of these indicators were present for surgical intervention [14]: Moderate or more severe pectus excavatum, evidence of limited or compressed cardiopulmonary function, severe psychosocial disorder and strong desire for surgical intervention by patients or parents. The details could be seen in our previous research [6–8].

Patients aged from 4 to 6 years old or 12–14 years old at the time of their primary Nuss procedure were included in the study. Children aged 4 to 6 were labeled as the preschool group, while those aged 12 to 14 were labeled as the adolescent group. Patients underwent routine preoperative preparation and all patients underwent conventional double incision Nuss surgery without thoracoscope (Fig. 1(A–F)). We usually choose to insert steel plates on the left side unless the patient shows significant right displacement of the heart. Chest radiographs were taken one day after surgery. We began collecting VAS pain scores every morning after the surgery on the second day. Participants with a score of three or less would be required to walk 100 m. An examination of the chest radiograph will be conducted on those who were able to independently completed the 100-m walking experiment without any discomfort. If there was no apparent pneumothorax, pleural effusion, or displacement of the steel plate, the patient would be discharged the next day.

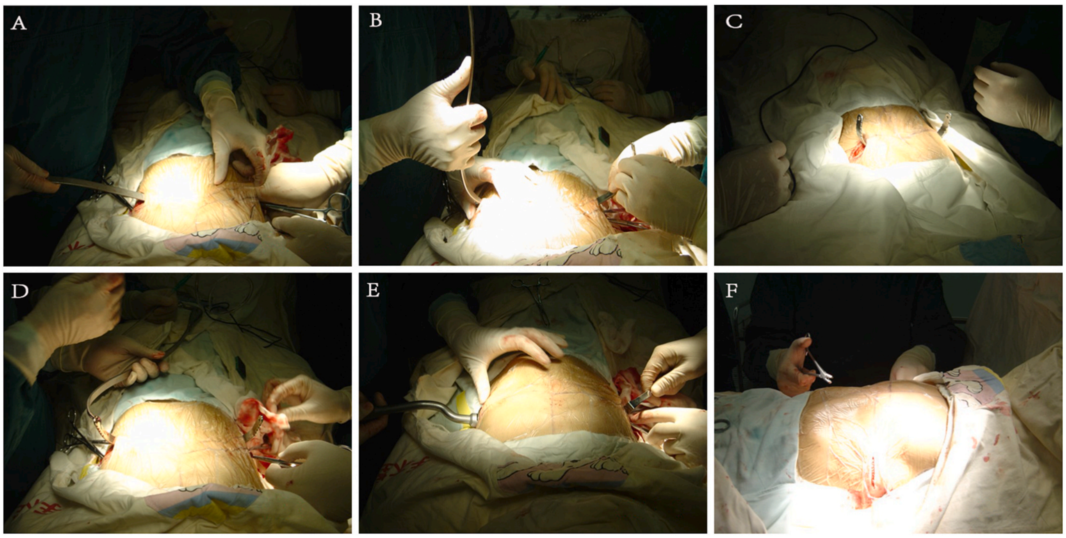

Fig. 1. Details of surgical procedure: A: Guide to establish a tunnel; B: Guiding steel plates through tunnels; C: Steel plate achievement placed behind the sternum; D: Flipped steel plate; E: Fine adjustment of steel plate position; F: Suture incision.

Patients were required to visit the outpatient clinic once a year until the age of 18 after the bar was removed. A satisfaction evaluation will be conducted during their last follow-up when they turn 18 years old.

The baseline time of the study was the first hospitalization time. The endpoint of the study was set as the last follow-up at the age of 18 in outpatient services. This study excludes patients with complex deformities, such as Marfan syndrome. During the study period, children who have undergone trauma or surgery that may affect chest shape will also be excluded. Patients with missing data will be excluded.

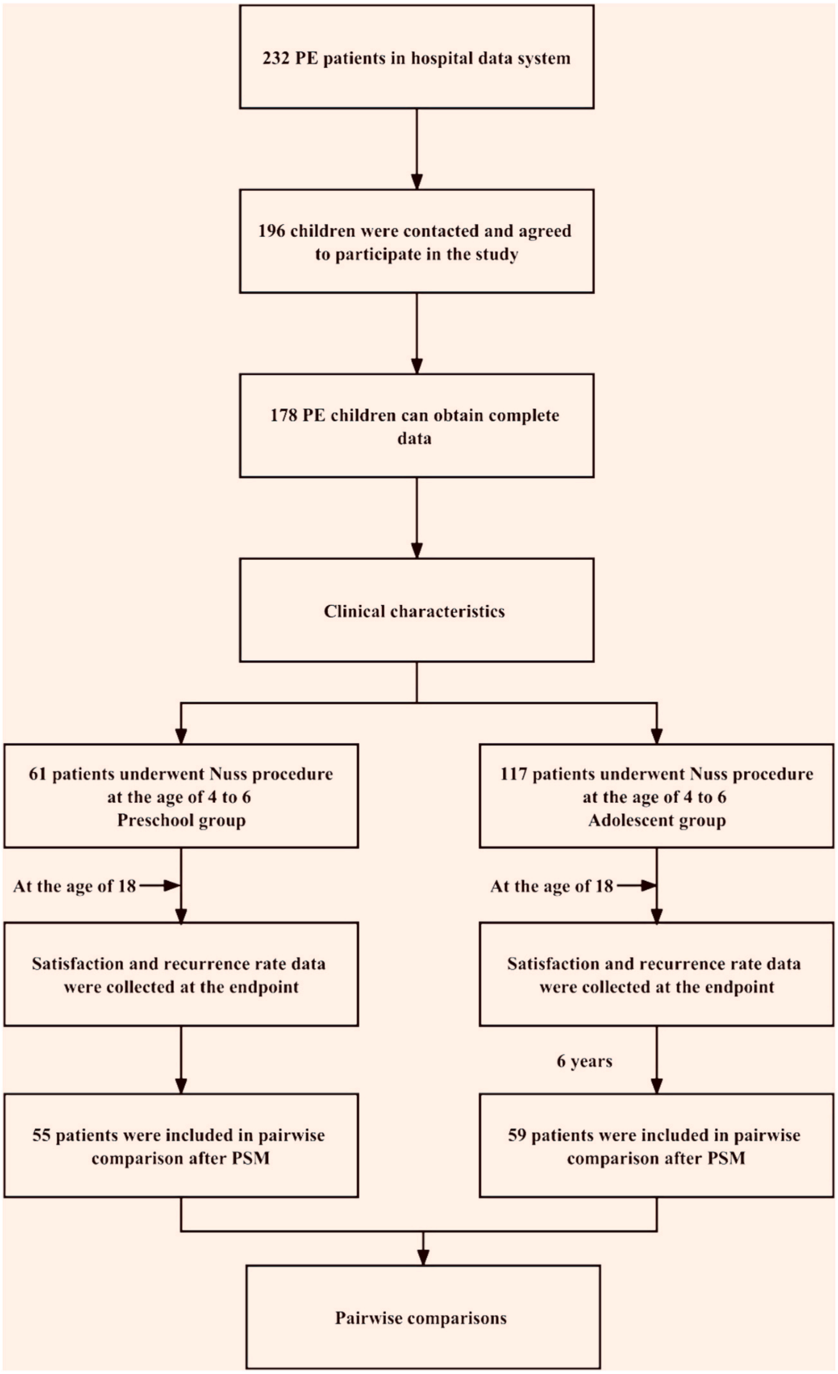

Fig. 2. Flow chart of the study: PSM: Propensity Score Matching.

2.2. Variables and outcome measures

A CT scan was used to calculate the HI. Abnormal lung function is defined according to the standards reported in our previous literature [8]. Prolapsed mitral valves or arrhythmias are regarded as abnormal cardiac function.

Complications of postoperative surgery included pneumothorax, pleural effusion, pneumonia, incision infection and bar displacement. We standardized the evaluation of analgesia dosage using oral machine equipment per kilogram (OME/kg) [15]. Detailed conversion information was described in Table S1. The satisfaction evaluation of the endpoint was conducted using the evaluation questionnaire proposed by Nuss himself. Patients reported that they were either"very happy" or "happy" with the results are recognized as satisfactory for the endpoint results [9]. Due to the lack of similar long-term research literature on children with pectus excavatum, the exact sample size cannot be estimated in advance.

2.3. Statistical analysis

When a data set is continuous, it is expressed as a mean and standard deviation (SD) for a normal distribution, or as a median with an interquartile range (IQR) for an abnormal distribution. In the presence of normally distributed continuous variables, an unpaired *t*-test was used to compare the differences between the two groups, whereas in the absence of normally distributed continuous variables, a Mann-Whitney *U* test was used. The Chi-square test was used to analyze categorical variables. The differences between groups were assessed using P values and standardized differences. Absolute balance is indicated by Standardized differences no more than 0.10.

To reduce potential bias between two different age groups, a propensity score matching (PSM) analysis was performed [16]. Specific relationships between the variables were examined using subgroup analysis, trend analysis, and a restricted cubic spline (RCS). We use mediation effect analysis to measure whether there are differences in long-term satisfaction among children of different age groups under different HI indices. Statistics were analyzed using SPSS version 24, Stata version 14.0, R and Python.

3. Results

In Fig. 2, the study flow chart is shown in detail. In the final analysis, 61 patients aged 4–6 years and 117 patients aged 12–14 years were included (Table 1). No differences were observed in variables of sex, HI, pulmonary function, and cardiac function. However, distribution of HI in the 4–6 years old group (Mean = 3.47, IQR = 3.21–4.02) was not well balanced compared with that in the 12–14 years old group (Mean = 3.27, IQR = 2.84–3.91, SMD = 0.143). The proportion of short-term complications in the 12–14 years old group was 17.95 %. No significant difference was observed compared with that in the 4–6 years old group (9/61, 14.75 %). The oral analgesic dosage of children in the 4–6 years old age group is significantly lower than that of the 12–14 years old group, and children in the younger age group are discharged earlier after surgery (mean = 6 days in 4–6 years old group versus mean = 7 days in 4–6 years old group). No significant difference in overall satisfaction and recurrence rate were observed between the two groups of children at the age of 18.

In order to reduce potential bias and make the baseline indicators of children more balanced between groups, we performed PSM according to variables of sex, HI, pulmonary function, and cardiac function. Fifty-five patients in the 4–6 years old group and 59 patients in the12 to 14 years old group were included after PSM. Variable imbalances were evidently reduced, and all indicators have reached the standard of well balanced (Fig. 3).

Table 1
Demographic and preoperative clinical characteristics.

Variable	Preschool 4–6 years old (n = 61)	Adolescent 12–14 years old (n = 117)	*P* value	Standardized differences
Sex	Male/Female (48/13)	Male/Female (96/21)	0.69	0.023[b]
Haller Index	3.47(3.21–4.02)	3.27(2.84–3.91)	0.23	0.143
Pulmonary Function	Normal/Abnormal (39/22)	Normal/Abnormal (82/35)	0.58	0.080[b]
Cardiac Function	Normal/Abnormal (44/17)	Normal/Abnormal (89/28)	0.29	0.021[b]
Complications	Yes/No (9/52)	Yes/No (21/96)	0.68	0.091[b]
Analgesia (OME/kg)	0.70(0.30–1.50)	1.80(1.20–3.05)	<0.001[a]	0.853
Hospital Stay post-surgery(D)	6(5–7)	7(6–8)	<0.001[a]	0.757
Recurrence (%)	4(6.5)	6(5.1)	0.73	0.063[b]
Endpoint Results	Satisfied/Unsatisfied (54/7) (88.5 %)	Satisfied/Unsatisfied (105/12)	0.80	0.042[b]

Abnormal lung function is defined as (FEV1) less than 80 % predicted value or FVC less than 80 % predicted value or FEV1/FVC less than 92 % predicted value.
Abnormal cardiac function is defined as mitral valve prolapse or arrhythmia.
PSM: Propensity score matching.
OME/kg: Oral Morphine Equivalents per kilogram.
[a] $P < 0.05$.
[b] Standardized differences less than 0.10 indicated absolute balance.

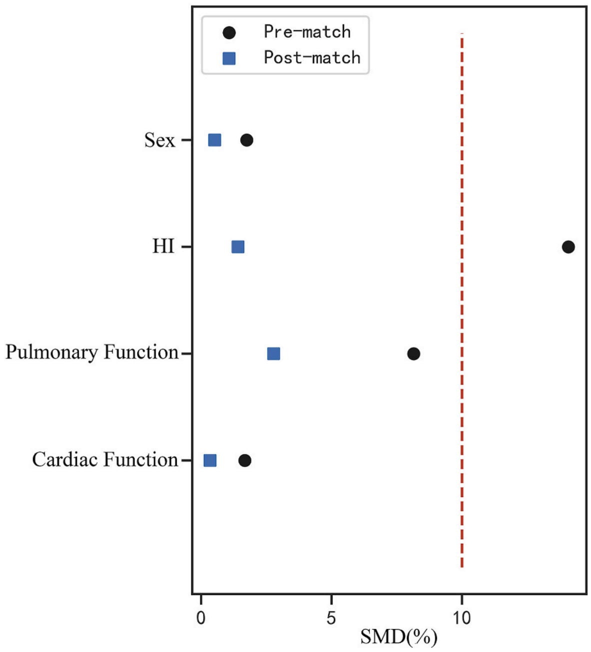

Fig. 3. Balance after Propensity Score Matching: PSM: Propensity Score Matching; SMD: Standard mean difference.

After PSM (Table 2), patients in 12–14 years old group require almost twice oral morphine equivalents (Mean = 1.50/kg, IQR = 0.90–2.30/kg) compared with those in 4–6 years old group (Mean = 0.70/kg, IQR = 0.30–1.50/kg, P < 0.001). The mean Hospital Stay post-surgery in 12–14 years old group was one day longer than that in 4–6 years old group (Mean = 7 days, IQR = 6–7/days, versus Mean = 6 days, IQR = 5–7/days, P = 0.001). No significance of hospitalization expenses was observed in two groups (P = 0.39).

Four patients in both groups experienced recurrence before the age of 18 and no statistical difference was observed. Both groups of children experienced 8 postoperative complications. In preschool group, 4 were diagnosed with pneumonia alone, 2 were with pneumothorax, 1 was with pleural effusion and 1was with incision infection. In adolescent group, 3 were diagnosed with pneumonia alone, 2 were diagnosed with pneumothorax. There is one patient each who suffered from pleural effusion, incision infection and bar displacement. Both children with wound infections were discharged on the seventh day after surgery, and subsequently underwent dressing changes at the outpatient clinic. The wound eventually healed without extra surgery, and both of them expressed dissatisfaction with the surgical treatment at the endpoint follow-up. A 13-year-old patient was followed up for one month after surgery and

Table 2
Demographic and preoperative clinical characteristics after PSM.

Variable	Preschool 4–6 years old (n = 55)	Adolescent 12–14 years old (n = 59)	*P* value	Standardized differences
Sex	Male/Female (43/12)	Male/Female (46/13)	0.69	0.010[b]
Haller Index	3.45(3.16–3.92)	3.44(3.05–3.91)	0.94	0.017[b]
Pulmonary Function	Normal/Abnormal (38/17)	Normal/Abnormal (40/19)	0.99	0.029[b]
Cardiac Function	Normal/Abnormal (40/15)	Normal/Abnormal (43/16)	0.99	0.004[b]
Complications	Yes/No (8/47)	Yes/No (8/51)	0.68	0.037[b]
Analgesia (OME/kg)	0.70(0.30–1.50)	1.50(0.90–2.30)	<0.001[a]	0.734
Hospital Stay post-surgery(D)	6(5–7)	7(6–7)	001[a]	0.620
Hospitalization expenses (RMB)	23846 (22231–25437)	24117 (22582–26219)	0.39	0.190
Recurrence (%)	4(7.2)	4(6.8)	0.99	0.157
Endpoint Results	Satisfied/Unsatisfied (49/6) (89.1 %)	Satisfied/Unsatisfied (52/7) (88.1 %)	0.99	0.031[b]

Abnormal lung function is defined as (FEV1) less than 80 % predicted value or FVC less than 80 % predicted value or FEV1/FVC less than 92 % predicted value.
Abnormal cardiac function is defined as mitral valve prolapse or arrhythmia.
PSM: Propensity score matching.
OME/kg: Oral Morphine Equivalents per kilogram.
[a] $P < 0.05$.
[b] Standardized differences less than 0.10 indicated absolute balance.

found a bar displacement. The parents requested observation. The patient finally removed the bar 2 years after surgery, but the shape was not good after removal. At the age of 17, the depression further worsened, and it was ultimately confirmed by CT examination as recurrence.

No statistical difference in recurrence rate (7.2 %, versus 6.8 %, P = 0.99) between the two groups. Six of 55 patients in 4–6 years old group recognized that the surgery did not achieve their expected results. In patients of 12–14 years old group, seven patients were dissatisfied with the Nuss procedure in their last follow-up when they reached the age of 18 (Fig. 4(A–C)). There is no significant difference in satisfaction rates between the two groups. (10.9 %, versus 11.80 %, P = 0.99).

In subgroup analysis, there is no difference in long-term satisfaction between the two groups of children under different HI indices (Table 3 and Fig. 5). In the trend analysis, there was no difference in long-term satisfaction among children in preschool group under different Haller index (P = 0.21). However, in adolescent group, as the HI index increases, overall satisfaction tends to decrease (P = 0.03). The reference point (HR/OR = 1) of Haller index was 3.47(P = 0.01) (Fig. 6).

In the analysis of mediating effects, we did not find any impact of changes in the HI index on the long-term satisfaction of the two groups(P = 0.87) (Table 4). The above results indicate that there is no significant difference in long-term satisfaction between the two groups of children at different severity levels.

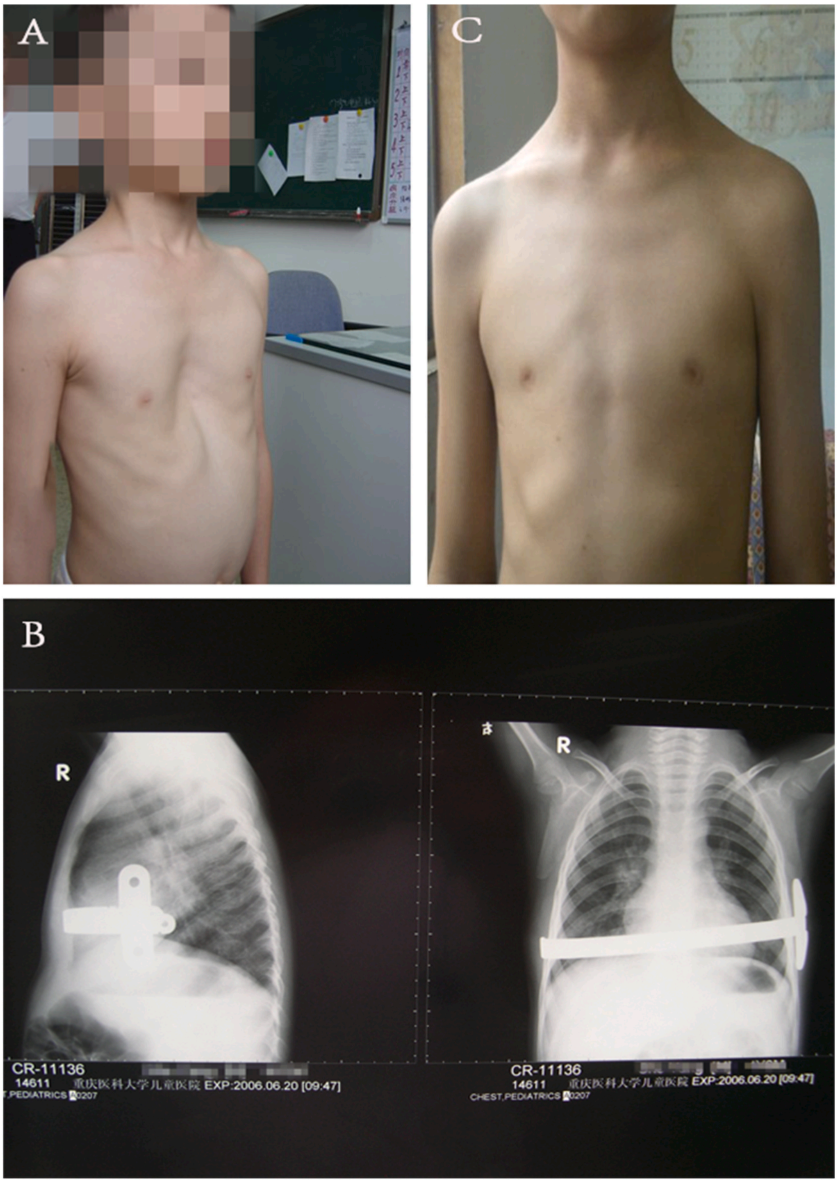

Fig. 4. Satisfaction of Long-term follow-up: A: Preoperative thoracic deformity of a boy aged four years and six months; B: X-ray results after Nuss producer. C: Appearance and morphology during follow-up at the age of 18.

Table 3
Subgroup analysis of long-term satisfaction under different HI indices.

HI	Total(N)	Total (Mean ± SD)	Preschool (N)	Preschool (Mean ± SD)	Adolescent (N)	Adolescent (Mean ± SD)	P value
2.40–3.03	23.000	0.957 ± 0.204	10.000	0.900 ± 0.300	13.000	1.000 ± 0.000	0.57
3.03–3.32	23.000	0.957 ± 0.204	12.000	1.000 ± 0.000	11.000	0.909 ± 0.287	0.42
3.32–3.61	24.000	0.875 ± 0.331	12.000	0.833 ± 0.373	12.000	0.917 ± 0.276	0.79
3.61–4.02	21.000	0.905 ± 0.294	10.000	1.000 ± 0.000	11.000	0.818 ± 0.386	0.63
4.02–6.33	23.000	0.739 ± 0.439	11.000	0.727 ± 0.445	12.000	0.750 ± 0.433	0.86

Preschool: patients underwent Nuss surgery at the age of 4–6 years old.
Adolescent: patients underwent Nuss surgery at the age of 12–14 years old.

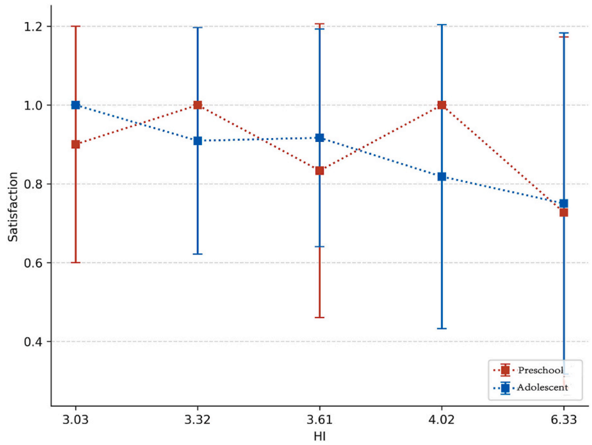

Fig. 5. RCS between Haller index and OR of Satisfaction: The reference point (HR/OR = 1) was 3.47 of HI.

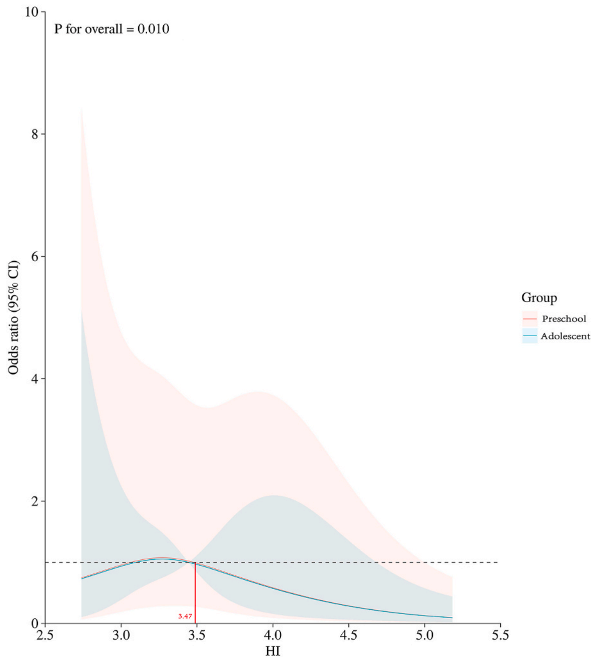

Fig. 6. Subgroup analysis of long-term satisfaction between the two groups of children under different HI indices.

Table 4
Analysis of mediating effects with HI, different age groups and long-term satisfaction.

Path	coef	se	pval	CI[2.5 %]	CI[97.5 %]	sig
HI -Group	−0.011	0.140	0.939	−0.287	0.266	No
Satisfaction -HI	−0.147	0.038	<0.001[a]	−0.222	−0.071	Yes
Group-HI- Satisfaction	−0.010	0.060	0.874	−0.129	0.110	No
Direct	−0.011	0.057	0.845	−0.124	0.101	No
Indirect	0.002	0.021	0.888	−0.041	0.044	No

[a] $P < 0.05$.

4. Discussion

The impairment of PE gradually aggravate and usually does not lead to life-threatening symptoms [17]. Therefore, there is no consensus on the most appropriate timing of surgery. Some surgeons consider the optimal timing is just before puberty (10–14 years old) because the bar can support the development of the chest during adolescence [10,18]. If only considering from the perspective of appearance repair, this age group may be the most appropriate.

However, the influence by pectus excavatum may occur early as most patients recognize the existence of deformities before the age of 6 [19]. It is important for surgeons to be aware that conditions such as pectus excavatum can lead to far greater disadvantage for patients than they realize. Many damages have already appeared before adolescence and are not easily improve after surgery. Our previous research confirmed that the incidence of psychosocial disorders in patients just before puberty was higher than that in 4-year--old patients [7]. Moreover, The development of academic performance is more conducive to surgical intervention immediately in PE children with definite surgical indications at 6 years old than observation [8].

Chinese Association of Thoracic Surgeons members reported that psychological disorders are the most common reason PE patients request surgery, with more than half of surgeons certifying this [2]. Considering the impact on psychological and behavioral development, it seems that the optimal surgical age for pectus excavatum should be advanced. The impact of PE on the physiological function of children will also manifest in the early stages. In primary school students, pectus excavatum is closely related to sleep-related breathing disorders with mean age of 9 years old [20]. For children over 11 years old, the resting pulmonary function was not significantly increased after surgery according to our previous research [21].

Perhaps performing surgery just before puberty is the safest decision for the surgeons, but ignoring the progression of psychological and physiological disorders in children makes no sense at any low recurrence rate. Do we place too much emphasis on the physical manifestations of the disease only? The technology of Nuss surgery has undergone significant improvements compared to the first decade. Steel plates and fixation devices are more reliable, and surgical techniques are also simplified. We have previously reported safety and efficacy in single incision non thoracoscopic assisted Nuss surgery [6]. Generally, most thoracic surgeons can master the Nuss procedure within 10 procedures of proctoring [22]. The recurrence rate of pectus excavatum surgery should be lower than that in the past. This study found that there was no statistically significant difference in the long-term postoperative recurrence rate between the 4–6 years old group and the 12–14 years old group. The overall long-term recurrence rate is about 7 %. Considering that these surgeries were completed more than 10 years ago, the long-term recurrence rate should be lower today.

Based on our previous research and the study, we believe that for children with surgical indications, around 6 years old may be the best time to undergo Nuss procedure. This stage of surgery is more conducive to the psychological and behavioral development [7] as well as academic performance [8], while not increasing the long-term recurrence rate and can reduce postoperative analgesic drug use.

We should also pay attention to some new technologies, such as Wang procedure. Wang procedure is a new type of modified sternal elevation with anterior sternal suspension technique reported in recent years for the treatment of pectus excavatum. This technology may be reliable for pectus excavatum, especially for those under 6 years old [23]. However, there is still a lack of long-term follow-up data to compare its advantages and disadvantages with Nuss procedure.

Another noteworthy issue is postoperative pain. Children at a young age have a relatively more malleable chest. As children get older, the strength of the sternum and ribs increases significantly. This study found that the dose of postoperative analgesics in hospital was lower in the younger age group than in the older age group. The average length of stay was also shorter for the younger age groups as well. The above results show that surgery at a younger age can lead to a better medical experience for patients. The evaluation questionnaire used in the study was proposed by Nuss himself, although the scale proposed by NUSS has been widely validated, there is still a gap between it and standardized quality of life scales such as the Quality-of-Life Scale of World Health Organization (WHOQOL-100) and36-item Short-Form (SF-36). In future research, we need to use more comprehensive quality of life scales to fully evaluate the long-term prognosis of patients.

Some limitation of the research should be mentioned. First is the limitation of population. This study is a single center study in western China. The conclusion of the study may not be generalizable to other regions. The second is that the patient's surgery year is relatively far from now. The long-term follow-up data at that time may not reflect the current situation, especially considering that we are currently using non thoracoscopic assisted single incision Nuss procedure. The third point is that this is a real-world study with follow-up time over 10 years. There may be some potential unknown factors that affect the outcome.

Based on the above limitations, we need to fully understand the potential biases that may exist in this real-world study. There are differences in the details of the Nuss technique used in different centers, including the selection of the number of incisions and whether thoracoscopy is used. Double incision fixation technique may be more reliable for adolescent children because their chest is harder.

The advancement of surgical techniques in the past decade may reduce the overall recurrence rate and length of hospital stay in pediatric patients, therefore the results of this study, such as recurrence rate and satisfaction, may be worse compared to the current clinical situation. The development of analgesic technology, especially the widely used cryoablation technique, may also result in a lower incidence of postoperative pain compared to the reported rate in this study.

However, to our knowledge, this is the first study that focuses on the long-term effects of surgery for pectus excavatum in preschool children and children just before puberty. The research provides evidence for surgeons that performing surgery at the age of 4–6 years old does not increase long-term recurrence rates and can reduce postoperative analgesic drug use in children with PE. The results of this study encourage surgeons to correct deformities of PE early rather than observing them.

5. Conclusion

For children with pectus excavatum, performing Nuss procedure at the age of 4–6 does not result in a higher long-term recurrence rate compared to Nuss surgery at the age of 12–14. Conversely, it and reduce the use of postoperative analgesics and length of hospital stay.

CRediT authorship contribution statement

Quan Wang: Writing – review & editing, Writing – original draft, Resources, Investigation, Funding acquisition, Data curation, Conceptualization. **Xiangpan Kong:** Visualization, Software, Formal analysis, Data curation, Conceptualization. **Chunian Ren:** Resources, Formal analysis, Data curation. **Zhengxia Pan:** Software, Resources, Project administration. **Chun Wu:** Validation, Supervision, Conceptualization. **Hongbo Li:** Visualization, Project administration, Conceptualization. **Yonggang Li:** Methodology, Data curation. **Gang Wang:** Software, Resources. **Jiangtao Dai:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of our hospital (approval number: 2021–42). Human participants involving in this study were protected according to the Helsinki Declaration, and each child's guardian signed an written authorization.

Consent for publication

All authors agree to publish.

Availability of data and materials

Data will be made available on request.

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Declaration of competing 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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39477.

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