



Early View

Research letter

Pectus excavatum is associated with sleep-related breathing disorders in children

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Pectus excavatum is associated with sleep-related breathing disorders
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Take home message;

By demonstrating the association between sleep-related breathing disorder (SRBD) and pectus excavatum (PE) in children, we identified SRBD as a possible risk for developing PE. All the clinician who found PE in children should consider SRBD screening.

To the editor:

Funnel chest or pectus excavatum (PE), is a chest wall deformity, and its major causes include hereditary connective tissue disorders and neuromuscular diseases [1-2]. In addition, PE is more likely to occur in the context of disorders associated with upper airway obstruction, including adenotonsillar hypertrophy, and bronchomalacia [3], suggesting that potential causal effects. Indeed, repeated increased intrathoracic negative pressure swings in children with sleep apnoea could lead to PE, although only limited evidence exists to this effect. We hypothesized that sleep-related breathing disorders (SRBD) is among the causes of PE in children, and therefore examined the association between PE and SRBD in children.

METHODS

As part of Matsuyama Children's Study which was conducted between 1 October 2014 and 31 March 2015 [4-5], a questionnaire was distributed to the caregivers of all 25,000 school children in Matsuyama City. Children at high risk for SRBD were reported as having at least one of the following sleep-related manifestations, including disrupted breathing for 2 to 7 nights a week, struggling to breathe at night for 2 to 7 nights a week, snoring for 5

to 7 nights a week, suddenly falling asleep for 3 to 7 nights a week, or loud snoring for 2 to 7 nights a week, or parental serious concerns on their child breathing during sleep conditions for 2 to 7 nights a week, and a total of 1,752 children which included all those children at high risk for SRBD were invited for a detailed interview and physical work-up.

The presence of PE was determined by visual inspection of the chest, along with assessment of the weekly frequency of disrupted breathing according to a previously validated questionnaire, that included some of the following questions [4, 6]; “Do you shake your child to breathe? ”, “Have you witnessed an apnoea during sleep? ”, or “Does your child struggle with breathing when asleep? ”.

A home-based overnight sleep monitoring was conducted, using a type-3 portable sleep monitor (Smart Watch®, PMP 300E, Philips Respironics GK, Eindhoven, Netherlands), which provided information on airflow limitation, based on which the respiratory disturbance event index (REI) was determined [7-8]. Variables included REI categories (REI <1, ≥1 to <2, ≥2/hour recording), age, Rohrer index, sex, the presence of adenotonsillar hypertrophy, presence of hay fever.

Of 1,752 invitations, 808 children agreed to participate in the present study and of those complete datasets of disrupted sleeping and PE were collected in 481 children and subjected to analysis. The participants were categorized into three groups based on the weekly frequency of disrupted breathing: never, 1 to 2, and 3 to 7 nights per week. The differences between the 3 groups were assessed using a generalized linear model, and multivariate odds ratios (OR) and 95% confidence intervals (95%CI) were assessed using a multivariate logistic regression model. P value <.05 was considered as reaching statistical significance. All statistical analyses were performed with SAS 9.04 software (SAS Institute Inc, Cary, NC).

The study protocol was reviewed and approved by Human Research Ethics Committee, Juntendo University.

RESULTS AND DISCUSSION

Children with disrupted breathing were more likely to have higher REI values, and a higher prevalence of adenotonsillar hypertrophy and PE (Table). Multivariate ORs (95%CI) for PE were 3.69 (1.52 to 8.98) and 3.81 (1.08 to 13.41) in children who reported disrupted breathing 1 to 2, and 3 to 7 nights per week, respectively, compared to the reference group (Table). These findings suggest that PE is associated with witnessed disrupted breathing, even when such reports occur only 1-2 times per week. In contrast, the rates of REI <1 , ≥ 1 to <2 , and ≥ 2 were 5.1%, 8.2% and 6.0% among the participants, respectively, whilst the multivariate-adjusted OR (95%CI) in children whose REI were ≥ 1 to <2 , and ≥ 2 , were 1.47 (0.51 to 4.27) and 0.88 (0.28 to 2.80), respectively, compared to those whose REI were <1 , suggesting that REI and PE were not associated. Interestingly, there is a dissociation between REI and disrupted breathing, raising several possibilities. Firstly, REI levels may be increased by the presence of central apnoea events, which are not accompanied by increased respiratory effort, but are frequently observed in children with obstructive sleep apnoea [9]. Second, children with obstructive sleep apnoea will exhibit increase

respiratory effort during sleep and may consequently develop PE.

Therefore, obstructed breathing, rather than greater REI values, is likely a major symptom associated with PE, as reported by another symptom, i.e., snoring, a condition that has also been noted for cognitive deficits in the context of SRBD [10]. Of note, an inordinately high prevalence of SRBD has been reported in children undergoing a sleep study before PE surgical repair [11].

There were several case reports showing that cor pulmonale accompanied PE, although children with PE rarely develop pulmonary hypertension [1]. A multi-center study in the US showed that spirometric parameters, such as FEV1 and FVC, were impaired in children with PE, but with a relatively small impact with reductions to the 85 to 90% of predicted values [3]. A study involving a cohort of infants born extremely preterm (The EPIC study) reported that higher prevalence of both PE and impaired spirometric function [12]. Furthermore, a follow-up observation on patients with life-long PE complained of low exercise tolerance and breathlessness, and other cardiopulmonary symptoms [13] and, in some patients, the symptoms of PE developed several decades later in life [13].

In some instances, such cardiopulmonary functional impairments may become symptomatic in the context of physical exercise [3], suggesting that PE may impose some restrictions on physical activity.

These studies and the current report suggest that PE is not only an aesthetic issue, but is also a condition associated with SRBD and adversely affecting aspects of respiratory function, and further expand on the evidence suggesting the diagnosis of SRBD when PE is observed during routine school physical assessments.

There are some limitations in this study; first, there is no widely accepted definition of PE, and the presence or absence of PE was identified by visual inspection only without any specific measurements [14], which may overestimate its prevalence. Second, since the participants of the detailed examination were selected, it is possible that children in the reference group may have underreported SRBD symptoms, potentially leading to underestimation of PE-SRBD association. In addition, there is no population-based epidemiologic data on the prevalence of PE in Japanese children, although the incidence of PE ranges from 0.2 to 0.4% in studies from the US or European countries [3]. The prevalence of PE in community children was

lower than that in the reference group of this study population, further reinforcing our assumptions on the association between PE and obstructed breathing. Finally, the present study was based on a cross-sectional design, and thus, precludes any inferences on causal relationship.

Collectively, increased intra-thoracic negative pressure swings as occur in SRDB may facilitate the progression of the PE chest wall deformity, and ultimately promote impaired life-long lung function [3, 12-13, 15].

CONCLUSION

The present study provides the first epidemiologic evidence regarding the association between PE and SRDB in children.

SUPPORT STATEMENT

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Table 1. Univariate & multivariate-adjusted odds ratio and 95% confidence intervals for pectus excavatum (PE), according to frequency of disrupted breathing during sleep.

disrupted breathing	Never	1 -2 days/wk	3-7 days/wk	p value
n (M:F)	301 (179:122)	140 (90:50)	40 (24:16)	
#age (year)	9.1 (1.7)	8.8 (1.6)*	9.2 (1.7)	0.04
#Rhorer index (Kg/m ³)	128.6 (20.5)	131.4 (22.3)	130.6 (21.3)	0.26
#REI (event/hr)	0.9 (1.8)	1.4 (2.8)*	1.6 (3.1)*	0.01
Adenotonsillar hypertrophy (%)	26.6	32.4	44.7*	0.02
hay fever (%)	32.2	46.7*	39.6	0.00
PE (M:F)	9 (6:3)	14 (13:1)	4 (3:1)	
univariate odds ratio	1.00	3.61 (1.52 - 8.55)	3.61 (1.06 - 12.30)	
##multivariate odds ratio	1.00	3.69 (1.52 - 8.98)	3.81 (1.08 - 13.41)	

#Data are presented as mean (\pm standard deviation), ##Multivariate adjusted with REI categories (REI<1, \geq 1 to <2, \geq 2/hour recording), age, Rohrer index, sex, the presence of adenotonsillar hypertrophy, presence of hay fever

+ indicates p value for difference between the three groups.

* indicates p value <.05 vs “never” group