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

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 these are potential causes of PE. 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 hypothesised that sleep-related breathing disorders (SRBDs) is among the causes of PE in children, and therefore examined the association between PE and SRDBs in children.

As part of the 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, Japan. Children at high risk for SRBDs were reported as having at least one of the following sleep-related manifestations, including disrupted breathing for two to seven nights a week, struggling to breathe at night for two to seven nights a week, snoring for five to seven nights a week, suddenly falling asleep for three to seven nights a week, or loud snoring for two to seven nights a week, or parental serious concerns on their child breathing during sleep conditions for two to seven nights a week. A total of 1752 children, which included all those children at high risk for SRBDs, 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 the following questions [4, 6]: "Do you shake your child to breathe?", "Have you witnessed an apnoea during sleep?" and "Does your child struggle with breathing when asleep?".

Home-based overnight sleep monitoring was conducted using a type-3 portable sleep monitor (Smart Watch PMP 300E; Philips Respironics GK, Eindhoven, the 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, $\geqslant 1$ to <2 or $\geqslant 2$ per hour of recording), age, Rohrer index, sex, the presence of adenotonsillar hypertrophy and the presence of hay fever.

Of 1752 invitations, 808 children agreed to participate in the present study and from those, complete datasets of disrupted sleeping and PE were collected in 481 children and subjected to analysis. The participants were categorised into three groups based on their weekly frequency of disrupted breathing: never, and one to two, or three to seven nights per week. The differences between the three groups were assessed using a generalised linear model, and multivariate odds ratios and 95% confidence intervals were assessed using a multivariate logistic regression model. $p<0.05$ was considered as reaching statistical significance. All statistical analyses were performed with SAS 9.04 software (SAS Institute Inc., Cary, NC, USA).

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By demonstrating the association between sleep-related breathing disorders (SRBDs) and pectus excavatum (PE) in children, SRBDs were identified as a possible risk for developing PE. All clinicians who find PE in children should consider SRBD screening. http://bit.ly/2LFS7yE

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The study protocol was reviewed and approved by the Human Research Ethics Committee, Juntendo University (Tokyo, Japan).

Children with disrupted breathing were more likely to have higher REI values, and a higher prevalence of adenotonsillar hypertrophy and PE (table 1). Multivariate odds ratios (95% CI) for PE were 3.69 (1.52–8.98) and 3.81 (1.08–13.41) in children who reported disrupted breathing one to two and three to seven nights per week, respectively, compared to the reference group (table 1). These findings suggest that PE is associated with witnessed disrupted breathing, even when such reports occur only one to two times per week. In contrast, the rates of REI <1, ⩾1 to <2 or ⩾2 events per h were 5.1%, 8.2% and 6.0% among the participants, respectively, whilst the multivariate adjusted odds ratios in children whose REIs were ⩾1 to <2 and ⩾2 events per h were 1.47 (0.51–4.27) and 0.88 (0.28–2.80), respectively, compared to those whose REIs were <1 event per h, 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 increased 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 SRBDs [10]. Of note, an inordinately high prevalence of SRBDs has been reported in children undergoing a sleep study before surgical PE repair [11].

There were several case reports showing that cor pulmonale accompanied PE, although children with PE rarely develop pulmonary hypertension [1]. A multicentre study in the USA showed that spirometric parameters, such as forced expiratory volume in 1 s and forced vital capacity, were impaired in children with PE but with a relatively small impact, with reductions to 85–90% of predicted values [3]. A study involving a cohort of infants born extremely preterm (the EPIC study) reported higher prevalence of both PE and impaired spirometric lung function [12]. Furthermore, a follow-up observation was that patients with life-long PE complained of low exercise tolerance and breathlessness, and other cardiopulmonary symptoms 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 also a condition associated with SRBDs and adversely affecting aspects of respiratory function, and furthermore, expand on the evidence suggesting the diagnosis of SRBDs 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

TABLE 1 Participant characteristics, and univariate and multivariate# adjusted odds ratios for pectus excavatum (PE), according to frequency of disrupted breathing during sleep

	Disrupted breathing			p-value¶
	Never	**One to two nights per week**	**Three to seven nights per week**	
Participants (male/female)	301 (179/122)	140 (90/50)	40 (24/16)	
Age years	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 events per h	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 (male/female)	9 (6/3)	14 (13/1)	4 (3/1)	
Univariate OR (95% CI)	1.00	3.61 (1.52–8.55)	3.61 (1.06–12.30)	
Multivariate# OR (95% CI)	1.00	3.69 (1.52–8.98)	3.81 (1.08–13.41)	

Data are presented as mean±SD unless otherwise stated. REI: respiratory disturbance event index. #: adjusted for REI categories (REI <1, ⩾1 to <2 and ⩾2 per h recording), age, Rohrer index, sex, the presence of adenotonsillar hypertrophy and the presence of hay fever. *: p<0.05 *versus* "never" group. ¶: for difference between the three groups.

is possible that children in the reference group may have underreported SRBD symptoms, potentially leading to underestimation of the PE–SRBD association. In addition, there are no population–based epidemiological 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 USA and 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 intrathoracic negative pressure swings as occur in SRDBs may facilitate the progression of the PE chest wall deformity and ultimately promote impaired life-long lung function [3, 12, 13, 15].

The present study provides the first epidemiological evidence regarding the association between PE and SRDBs in children.

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