

Oximetry-detected pulsus paradoxus predicts for severity in paediatric asthma

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/archdischild-2019-318043>).

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Received 6 August 2019

Revised 10 January 2020

Accepted 5 February 2020

Published Online First

24 February 2020



► <http://dx.doi.org/10.1136/archdischild-2020-318936>



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To cite: G Krishnan S, Wong HC, Ganapathy S, et al. *Arch Dis Child* 2020;**105**:533–538.

ABSTRACT

Objective To evaluate if qualitative visual detection of pulsus paradoxus (PP) on the pulse oximeter plethysmograph can predict outcomes for children with moderate to severe respiratory distress in a paediatric emergency department (ED).

Design Prospective cohort study.

Setting Paediatric ED of a tertiary paediatrics hospital in Singapore.

Patients Children managed for moderate to severe wheezing in the resuscitation bay of the ED.

Interventions Patients were assessed for the presence of PP based on visual detection of oximeter plethysmograph before and after initial inhaled bronchodilator therapy.

Main outcome measures These include the need for adjunct medications such as aminophylline or magnesium sulfate, the need for supplementary ventilation and the need for admission to the high dependency unit (HDU) or intensive care unit (ICU).

Results There were 285 patients included in the study, of whom 78 (27.4%) had PP at ED presentation. There were 40 (14.0%) who had PP after initial management. Children who had PP after initial management had significantly relative risks (RR) of requiring adjunct medications (RR 12.5, 95% CI 4.0 to 38.6), need for supplementary ventilation (RR 5.6, 95% CI 1.2 to 26.5) and admission to the HDU/ICU (RR 5.6, 95% CI 3.0 to 10.4).

Conclusion Qualitative detection of PP on pulse oximetry can be used as a potential point-of-care tool to help in the assessment of response to initial treatment in paediatric patients with acute moderate to severe asthma exacerbations. Future studies are needed to assess and validate its role in guiding ED management of acute paediatric asthma.

INTRODUCTION

Asthma is one of the most common reasons for paediatric emergency department (ED) visits.¹ The severity of asthma exacerbations is often assessed based on subjective clinical indicators. Asthma severity scores such as the Pediatric Respiratory Assessment Measure² and the Pediatric Asthma Severity Score (PASS)³ have been shown to be valid in gauging the severity of an exacerbation. Although interobserver reliability has been shown with these scoring tools, they too involve subjective clinical assessment.

International guidelines state that peak expiratory flow rate (PEFR) is a more valid measure of airway obstruction. However, PEFR is difficult to obtain in an acute setting or in children younger

What is already known on this topic?

- Asthma is one of the most common reasons for attendance to the paediatric emergency department (ED).
- There is a need for ED physicians to efficiently manage these patients and for accurate allocation of appropriate resources.
- Studies have shown the quantitative assessment of oximeter plethysmograph variability, as a surrogate for pulsus paradoxus (PP), can be used to assess severity of asthma.

What this study adds?

- First study to use qualitative assessment of plethysmograph variability on non-specialised, bedside physiological monitors to detect presence of PP to prognosticate moderate to severe acute asthma exacerbation in children.
- Presence of PP at ED presentation has good correlations with acute clinical severity using Pediatric Asthma Severity Score.
- Presence of PP after initial inhaled bronchodilator therapy has a higher relative risk for needing adjunct medications (aminophylline/magnesium sulfate) and for needing admission to high dependency and intensive care units.

than 5 years who may be too ill or too young to perform the test accurately. There are few other objective measures to assess the severity of asthma.⁴

Pulsus paradoxus (PP) is an objective bedside measurement for assessment of airway obstruction and response to treatment. Adolf Kussmaul first defined PP in 1873⁵ as a decrease in systolic blood pressure of more than 10 mm Hg during inspiration. Patients with obstructive airway disease have a loaded inspiration due to difficulty in exhalation, causing a fall in intrathoracic pressure, which causes an increase in right ventricular diastolic volume and stroke volume.⁶ During expiration, the left ventricular diastolic volume and stroke volume increase while the right ventricular volumes return to baseline values. This causes variability of the systolic blood pressure during inspiration and expiration.^{7,8}

PP is traditionally measured using a sphygmomanometer or intra-arterial catheter,⁹ both of which are infrequently used in the ED. Pulse oximeters give a qualitative display of the pulse amplitude of the vascular bed underlying the probe.¹⁰ Recent

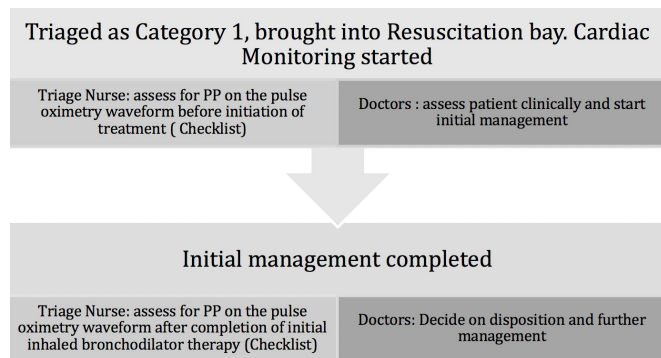


Figure 1 Sequence of assessment for PP on pulse oximetry. PP, pulsus paradoxus.

studies demonstrated that such plethysmograph waveforms accurately represent the peripheral arterial waveform and can be used to estimate the degree of PP where a greater degree of PP correlates with higher asthma severity.

The aim of this study is to investigate if qualitative visual detection of PP on the pulse oximeter plethysmograph (which is based on a regular respiratory variation in the amplitude of the waveform) can be used to predict outcomes for children attending the ED) with moderate to severe respiratory distress. We excluded children with mild wheeze as clinical evaluation is sufficient, and additional assessment or prognostic tools are unlikely to provide further clinical utility.

METHODOLOGY

Patients

This is a single-centre study conducted prospectively in the ED of a tertiary care children's hospital from December 2014 to May 2015. We included children aged up to 16 years who attended the ED with moderate to severe respiratory distress and who were triaged as category 1. Patients less than 24 months of age with no history of recurrent wheeze or asthma and those with the diagnoses of pleural effusions, croup, anterior mediastinal tumours and anaphylaxis were excluded. Patients were also excluded if they could not be assessed for PP before starting treatment.

Study design

Patients presenting to the ED were first triaged by nurses according to the Singapore Paediatric Triage Scale (online supplementary appendix 1). Patients with respiratory distress and who needed to be seen with immediate priority were triaged as category 1 as per the department's triage guidelines (online supplementary appendix 2). They were brought into the resuscitation bay and put on cardiorespiratory monitoring (Phillips Intellivue MP30 cardiac monitor). The triage nurse immediately assessed the pulse oximeter plethysmographic waveform on the cardiac monitor to detect the presence of PP (figure 1). This was documented on a PP data sheet.

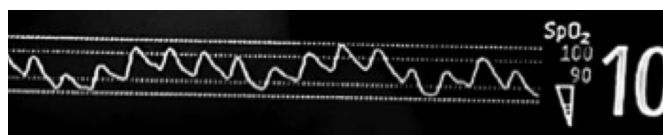


Figure 2 Plethysmographic variability in a child with pulsus paradoxus.

The patient was then managed by a team of ED physicians according to the clinical severity of respiratory distress. Management was standardised according to the department's guidelines (online supplementary appendix 3). Initial resuscitative management included bronchodilators (inhaled Salbutamol and Ipratropium bromide) administered through a metered dose inhaler or nebuliser, and oral or intravenous steroids. Adjunct medications such as intravenous magnesium sulfate or aminophylline were administered for refractory respiratory distress or status asthmaticus after initial inhaled bronchodilator therapy.

After the initial set of two to three cycles of intensive inhaled bronchodilator therapy, the same triage nurse again assessed the pulse oximeter plethysmographic waveform for PP and documented it on the PP datasheet. This datasheet was collected at the end of the treatment and analysed.

During the entire resuscitation, the ED physicians were not aware of the data or documentation of PP so as not to alter the patient assessment or management. Within 2 hours of triage, the physicians would make a decision on the disposition of the child from the ED based on the patient's clinical severity and the level of further treatment required.

Determination of pulsus paradoxus

PP was taken to be qualitatively present if there was a regular variation in the amplitude of the plethysmographic waveform in accordance with the respiratory cycle of the patient (figure 2).

Triage nurses were trained to detect PP on the waveform (online supplementary appendix 4). By the time the study commenced, the triage nurses were confident and consistent in their assessments of the pulse oximeter plethysmograph.

Doctors in the department were aware of the ongoing study but were not trained in the evaluation of the pulse oximetry detection of PP. The teaching sessions on recognising PP on pulse oximetry included only the nurses. In our department, it is not part of our assessment tools to use PP as a measure of our asthma assessment and therefore our asthma management guidelines do not depend on the presence of PP.

Outcomes measured

The primary outcomes measured include the need for adjunct medications such as aminophylline or magnesium sulfate, the need for supplementary ventilation such as non-invasive positive pressure ventilation (continuous/bilevel positive airway pressure) or endotracheal intubation, and the need for admission to the high dependency unit (HDU) or intensive care unit (ICU). The outcomes were compared for those with PP at arrival at the ED and those with PP after initial inhaled bronchodilator therapy.

Data collection and statistical analysis

Data were reviewed from electronic medical records as well as from the PP data sheets, which were filled by triage nurses and deposited into a collection box.

Fisher's exact probability test was used to see whether there were significant differences between the PP group and those without PP at ED presentation prior to treatment in terms of demographics, the patients' history of wheezing, the patients' history of admission to high dependency or ICU and the patients' history of use of preventers. Mann-Whitney U test was performed to see whether there were significant differences in age and PASS between those with PP and those without PP at ED presentation. Fisher's exact probability test was carried out to see whether there were significant statistical differences in tachypnoea (based on age), oxygen saturation, use of adjuncts,

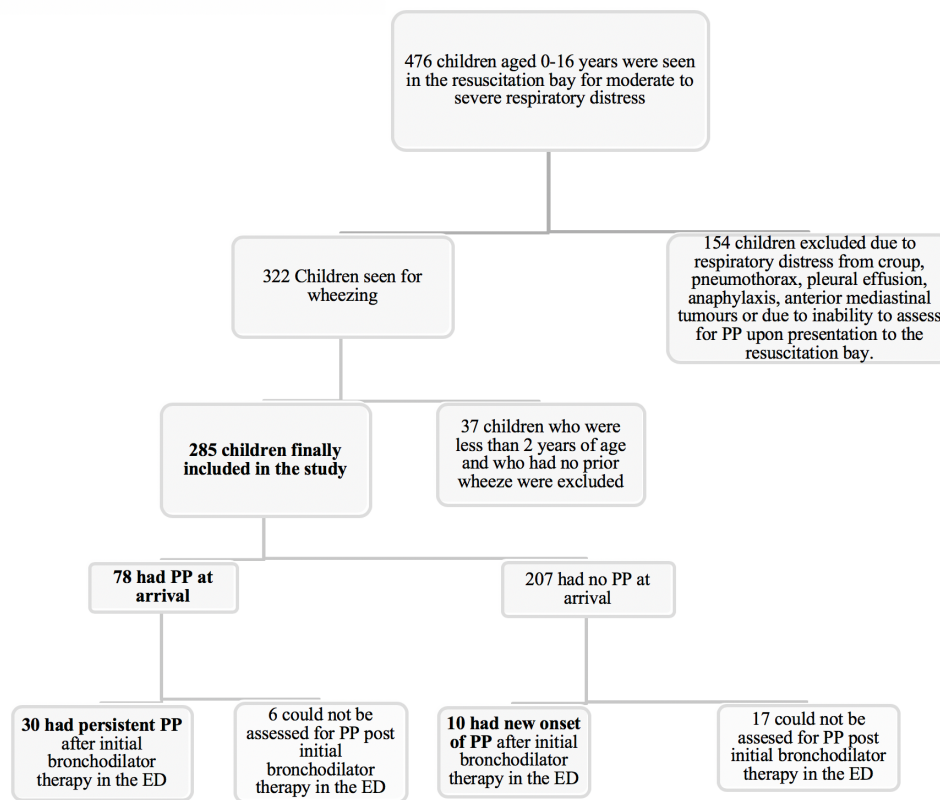


Figure 3 Flowchart of patients included in study. ED, emergency department; PP, pulsus paradoxus.

need for supplementary ventilation (non-invasive ventilation or endotracheal intubation) and need for high dependency or ICU care between the PP group and those without PP at ED presentation, and whether there were significant statistical differences in the use of adjuncts, the need for supplementary ventilation and the need for high dependency or ICU care between the PP group and those without PP after initial management. Statistical significance was set at 5%. Statistical analyses were performed using IBM SPSS Statistics V.25 (IBM, Armonk, New York, USA).

RESULTS

A total of 476 patients were seen for moderate to severe respiratory distress in the resuscitation bay of our ED during the study period. Of these, 37 patients were excluded for being less than 24 months of age and with first presentation of wheeze and 154 patients were excluded from the analysis for having respiratory distress due to croup, pneumothorax, pleural effusion, anaphylaxis, anterior mediastinal tumours or due to inability to assess for PP at arrival (figure 3). Of the remaining 285 patients who were included in the study, 78 (27.4%) were assessed to have PP at arrival. There were no significant differences between the PP group and those without PP at arrival in terms of demographics and the patients' wheezing histories (table 1). Study participants were primarily in early childhood and mainly of Chinese race. There was also no significant difference in the degree of hypoxia but patients with PP at arrival were significantly found to have higher PASS (table 2). PP at arrival was significantly associated with more severe asthma with PASS of 4–6, $p < 0.001$ (table 3).

Patients who presented with PP at arrival were found to have higher relative risk (RR) of requiring adjunct medications such as aminophylline and magnesium sulfate (RR 3.0, 95% CI 1.1 to 8.1; $p = 0.033$) and admission to HDU/ICU (RR 2.1, 95% CI

Table 1 Demographics of patients presenting to ED with moderate to severe wheezing

	PP present at arrival in ED (n=78)	PP absent at arrival in ED (n=207)	P value
Median age (25th–75th percentile)	3.86 (2.45–5.38)	3.55 (2.18–5.89)	0.535
Age			
Number of children <1 year of age	3 (3.8%)	15 (7.2%)	0.637
Number of children 1–2 years old	9 (11.5%)	26 (12.6%)	
Number of children >2 years old	66 (84.6%)	166 (80.2%)	
Race			
Chinese	33 (42.3%)	91 (44.0%)	0.728
Malay	28 (35.9%)	82 (39.6%)	
Indian	11 (14.1%)	22 (10.6%)	
Others	6 (7.7%)	12 (5.8%)	
Gender			
Male	46 (59.0%)	114 (55.1%)	0.594
History of previous admission to HDU or ICU	9 (11.5%)	16 (7.7%)	0.349
History of use of preventers (inhaled corticosteroids or montelukast)	9 (11.5%)	47 (22.7%)	0.044
Details of pretreatment received prior to ED attendance			
No pretreatment	33 (42.3%)	104 (50.2%)	0.496
Inhaled Salbutamol given via MDI space chamber	36 (46.2%)	83 (40.1%)	
Nebulised bronchodilators	9 (11.5%)	20 (9.7%)	

P value of less than 0.05 is considered significant.

ED, emergency department; HDU, high dependency unit; ICU, intensive care unit; MDI, metered dose inhaler; PP, pulsus paradoxus.

Table 2 Respiratory status on presentation to the ED

	PP present (n=78)	PP absent (n=207)	P value
Tachypnoea present	76 (97.4%)	201 (97.1%)	1
Oxygen saturation			
≥95%	29 (37.2%)	78 (37.7%)	0.274
92%–94%	36 (46.1%)	78 (37.7%)	
<92%	13 (16.7%)	51 (24.6%)	
Median (IQR) PASS*	5.00 (4.00–5.00)	3.00 (3.00–5.00)	<0.001

P value of less than 0.05 is considered significant.

*PASS scoring includes wheeze, work of breathing and prolonged expiratory phase. ED, emergency department; PASS, Pediatric Asthma Severity Score; PP, pulsus paradoxus.

1.1 to 3.9; $p=0.025$) (table 4). However, there was no significant difference in the requirement for supplementary ventilation ($p=0.351$).

There were 23 patients with unavailable information on PP after initial bronchodilator therapy in the ED. Of the remaining 262 patients, 30 (41.7%) of the patients who presented with initial PP had persistence of PP after initial bronchodilator therapy in the ED, while 10 patients (5.3%) who did not have PP initially were assessed to have PP after initial bronchodilator therapy. These 40 patients who had PP after initial bronchodilator therapy were found to have a significantly greater risk of requiring adjunct medications (RR 12.5, 95% CI 4.0 to 38.6; $p<0.001$), need for supplementary ventilation (RR 5.6, 95% CI 1.2 to 26.5; $p=0.048$) and admission to the HDU/ICU (RR 5.6, 95% CI 3.0 to 10.4; $p<0.001$) (table 5).

DISCUSSION

Our study showed that children with PP, before and after initial inhaled bronchodilator therapy had a higher risk of requiring adjunct medications and admission to HDU/ICU.

Many studies have successfully demonstrated the phenomenon of PP in patients with severe airways obstruction.^{6 11 12} Recently, studies have shown correlations between the quantitative variability in pulse oximeter plethysmograph and PP measured via traditional methods of sphygmomanometer and intra-arterial blood pressure monitoring.⁹ For example, Wright *et al* compared finger arterial pressure monitors to the patient's respiratory cycles to determine the high and low blood pressure measurements during that time frame.¹³ Hartet *et al* measured respiratory waveform variations precisely in millimetres in patients requiring mechanical ventilation and correlated this with PP.¹⁴ On the other hand, Arnold *et al* estimated PP by calculating the area under the curve of a plethysmograph tracing and compared this with FEV₁.¹⁵ These different methods have successfully shown correlations between PP detected by pulse oximetry and existing criterion standards.

However, these methods are challenging to use in a time-critical setting such as the ED. To our knowledge, the use of qualitative detection of PP to predict outcomes has not been investigated before. Our study is the first of its kind in showing that simple pattern recognition of PP on pulse oximeter plethysmograph can be used to predict outcomes and hence guide management of children with moderate to severe respiratory distress.

Brandwein *et al*¹⁶ found a significant difference in the degree of PP between children discharged home versus children admitted to the hospital. They studied the Pleth Variability Index, which is a ratio of the calculated difference in maximum and minimum amplitude of the plethysmograph waveform and the maximum amplitude.¹⁶ Though our study did not evaluate the exact degree of PP, we had similar findings of a higher RR of getting admitted to HDU/ICU among those detected to have PP on the plethysmograph after initial management. This shows that even without assessing the exact degree of PP, outcomes may be predicted on qualitative visual assessment of PP and it is an easy point-of-care assessment technique which does not involve additional special equipment and can be performed by anyone trained to recognise patterns. It can also be a useful and objective prognosticating tool, which can be easily performed even in children younger than 5 years or those who are too ill to comply with spirometry.

Different studies have measured the PP on plethysmography at different time points. In particular, Wright *et al* compared the degree of PP at three time points: before initiation of treatment, at 30 min and at 60 min after treatment. Their study found that the PP was significantly higher for the poor outcome groups compared with good outcome groups at all measurement times.¹³ In our study, we found that while the need for adjunct medications and the need for admission to HDU/ICU were higher in both the PP groups before and after initial management, the RR for these outcomes was much higher in the group with persistent PP after initial bronchodilator therapy. This could be attributed to the presence of persistent severe asthma and bronchospasm that is refractory to initial management, which creates a greater need for adjunct medications and for closer monitoring in HDU/ICU, whereas those who show resolution of PP could have had a reversal of bronchospasm with initial management and therefore have a lower risk for requiring HDU/ICU admission. We acknowledge the limitations given the low frequencies of these clinical outcomes.

In our study, we found that those with PP at arrival had higher PASS than those without. Although interobserver reliability has been shown with using PASS, there is a certain degree of subjectivity in its assessment. Assessment of PP on plethysmograph can be easily done using non-specialised besides physiological monitors and provide an additional tool when assessing children with moderate to severe asthma.

There are areas for improvement in our study. In our study, only one triage nurse assesses PP on pulse oximetry. This can

Table 3 Predictive value of oximetry-detected pulsus paradoxus at arrival on severity of acute asthma based on PASS

Severity (PASS*)	PP present (n=78)	PP absent (n=207)	P value	PPV (%) (95% CI)	NPV (%) (95% CI)	LR+ (95% CI)	LR- (95% CI)
Mild (0)	0	0	<0.001	87.2 (77.7 to 93.7)	57.5 (50.4 to 64.3)	5.6 (3.0 to 10.5)	0.6 (0.5 to 0.7)
Moderate (1–3)	10 (12.8%)	119 (57.5%)					
Severe (4–6)	68 (87.2%)	88 (42.5%)					

P value of less than 0.05 is considered significant.

*PASS scoring includes wheeze, work of breathing and prolonged expiratory phase.

LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; PASS, Pediatric Asthma Severity Score; PP, pulsus paradoxus; PPV, positive predictive value.

Table 4 Associations of oximetry-detected PP, at ED presentation, with primary outcomes

	PP present (n=78)	PP absent (n=207)	Relative risk (95% CI)	P value
Use of adjuncts (intravenous MgSO ₄ , aminophylline)	8 (10.3%)	7 (3.4%)	3.0 (1.1 to 8.1)	0.033
Need for supplementary ventilation (non-invasive or endotracheal intubation)	3 (3.8%)	3 (1.4%)	2.7 (0.6 to 12.9)	0.351
Need for HDU or ICU care	15 (19.2%)	19 (9.2%)	2.1 (1.1 to 3.9)	0.025

P value of less than 0.05 is considered significant.

ED, emergency department; HDU, high dependency unit; ICU, intensive care unit; MgSO₄, magnesium sulfate; PP, pulsus paradoxus.

Table 5 Associations of oximetry-detected PP, after initial inhaled bronchodilator therapy, with primary outcomes

	PP present (n=40)	PP absent (n=222*)	Relative risk (95% CI)	P value
Use of adjuncts (intravenous MgSO ₄ , aminophylline)	9 (22.5%)	4 (1.8%)	12.5 (4.0 to 38.6)	<0.001
Need for supplementary ventilation (non-invasive or endotracheal intubation)	3 (7.5%)	3 (1.4%)	5.6 (1.2 to 26.5)	0.048
Need for HDU or ICU care	15 (37.5%)	15 (6.8%)	5.6 (3.0 to 10.4)	<0.001

P value of less than 0.05 is considered significant.

*23 patients could not be assessed for presence of pulsus paradoxus after initial inhaled bronchodilator therapy.

HDU, high dependency unit; ICU, intensive care unit; MgSO₄, magnesium sulfate; PP, pulsus paradoxus.

give rise to interobserver variability. Though we tried to mitigate this limitation through adequate training and testing of the triage nurses, it would still be useful to get two nurses in future studies to improve reproducibility and limit potential variability.

In addition, another limitation is the risk of observer bias as the doctors in the department were aware of the ongoing study and complete blinding of the physicians was not feasible. We attempted to mitigate the observer bias by training only the nurses (and not the doctors) on the detection of PP on pulse oximetry. However, it would be worthwhile to consider doing a similar study in a multicentre trial with blinding of the physicians to assess interobserver variability and to assess the outcomes of children with severe wheezing.

Despite our findings, it is important to note that detection of PP on plethysmography should not replace clinical judgement. Nevertheless, after initial bronchodilator therapy, if PP is still noted on the plethysmography, it may be used as an additional clinical adjunct in the evaluation of the severity of wheeze and guide further management in refractory cases of bronchospasms and status asthmaticus.

CONCLUSION

Qualitative detection of PP on pulse oximetry can be used as a potential point-of-care tool to help in the assessment of response to initial treatment in paediatric patients with acute moderate to severe asthma exacerbations. Future studies are needed to assess and validate its role in guiding ED management of acute paediatric asthma.

Acknowledgements We would like to acknowledge the triage nurses at the department of emergency medicine in KK Women's and Children's Hospital, Singapore for their contribution in filling up the pulsus paradoxus data collection sheet before and after initial bronchodilator therapy for each study participant.

Contributors SGK contributed substantially in the methodological design, collecting the data, interpretation of the data, drafting the work and agreeing to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. She approves of the final version to be published. HCW helped in analysis and interpretation of data for the work, revising the work critically for important intellectual content and in approving the final version to be published. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. She approves of the final version to be published. SG contributed substantially in the methodological design, collecting the data, interpretation of the data, the analysis and interpretation of data for the work, revising the manuscript critically for important intellectual content and in approval of the final version to be published. He agrees to be accountable for all aspects of the work in ensuring

that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. He approves of the final version to be published. GY-KO conceived the presented idea, substantially contributed to the methodological design, analysis and interpretation of data for the work, revising the manuscript critically for important intellectual content and in approval of the final version to be published. He agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. He approves of the final version to be published.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Approval was obtained from the local SingHealth Centralised Institutional Review Board (CIRB) prior to commencement of the study. The CIRB approval number is 2014/091/E.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The corresponding author (Sandhya G Krishnan, sandhya.gkrishnan@mohh.com.sg) has stored the deidentified patient data in a password-locked desktop computer and can provide the data on request.

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