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Research article

Discrepancy between arterial oxygen saturation and pulse oximetry measurement in a Chinese pediatric patient cohort

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ABSTRACT

Background: Increasing evidence suggest a racial bias in pulse oximetry measurement, but this was under investigated in Asian pediatric populations.

Methods: Via the Pediatric Intensive Care database, this retrospective study included pediatric patient records of arterial oxygen saturation (SaO_2) and oxygen saturation on pulse oximetry (SpO_2) measured within 10 min. Discrepancy was examined, and potential predictors of occult hypoxemia (defined as SaO_2 <88% with the paired SpO_2 ≥92%) as well as its association with outcomes were explored by logistic regression.

Results: A total of 390 patients were included with 454 pairs of SaO_2-SpO_2 readings. The study population consisted of Han Chinese (99.0%) and 43.6% were female. Occult hypoxemia was observed in 20.0% of the patients, with a mean SaO_2 of 71.4 ± 15.8%. Potential predictors of occult hypoxemia included female, being first admitted to cardiac ICU, congenital heart disease, increased heart rate, while patients with prior surgery records were less likely to experience occult hypoxemia. Patients with occult hypoxemia had numerically higher in-ICU mortality (16.7% versus 10.9%) and in-hospital mortality (17.9% versus 10.9%), but the associations were not statistically significant.

Conclusions: There was a substantial proportion of hypoxemia that was not detected by pulse oximetry in the Chinese pediatric patients, which might be predicted by several characteristics and seemed to associate with mortality.

1. Introduction

Pulse oximetry is routinely used in clinical practice for measuring oxygen saturation to detect hypoxemia and guide oxygen therapy [1]. The basic rationale of pulse oximetry is that oxygenated hemoglobin and deoxygenated hemoglobin absorb light at different wavelengths, based on which oxygen saturation can be calculated by measuring absorption of different wavelengths after the light passes through the tissues [2]. Since skin pigmentation also affects absorption of light [3], and the pulse oximeter technology was not originally developed in a racially diverse population [4], there are increasing concerns about potential racial bias of pulse oximetry

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measurement. Although a few studies reported a null association [5,6], most studies in various healthcare settings consistently showed patients with darker skin color saw greater discrepancy between arterial oxygen saturation (SaO_2) and pulse oximetry measurement (SpO_2), leading to increased risk of occult hypoxemia [4,7–14], which was associated with delayed care and unfavored outcomes [15–20]. Although Asian population was underrepresented among these studies (which often employed race/ethnicity as a proxy for skin pigmentation), they seemed to be less affected by this issue (than Black people) [18,19]. However, for pediatric patient populations, evidence about potential racial bias of pulse oximetry measurement was much more limited and with inconsistent findings [3,21–24], and as far as we know, none of them included Asian pediatric patients, presenting a knowledge gap. Given the popular use of pulse oximetry measurement in practice and the clinical relevance of occult hypoxemia, in the current study we examined discrepancy between SaO_2 and SpO_2 in a Chinese pediatric patient cohort, including its predictors and association with clinical outcomes.

2. Materials and methods

2.1. Data source

The study used data from the Pediatric Intensive Care (PIC) database (version 1.1.0), which comprises information of pediatric patients (i.e., age ≤18 years) who were admitted to intensive care units (ICUs) between 2010 and 2018 at a large children's hospital in China (i.e., the Children's Hospital, Zhejiang University School of Medicine, China). The original project that developed the PIC database was approved by the Institutional Review Board (IRB) of the Children's Hospital, Zhejiang University School of Medicine, and the requirement for individual patient consent was waived because the project did not impact clinical care, and all protected health information was deidentified. More details about the database were previously described [25].

The database was publicly accessible after completing the required steps for data access, and all data were deidentified already. QC had data access, and the current study was also further approved by the IRB of the Guangdong Provincial People's Hospital (No. KY2023-225). We used data about vital sign measurements, laboratory measurements, diagnostic codes, length of hospital stays, and survival. The study complied with the Helsinki Declaration 1964 and its later amendments.

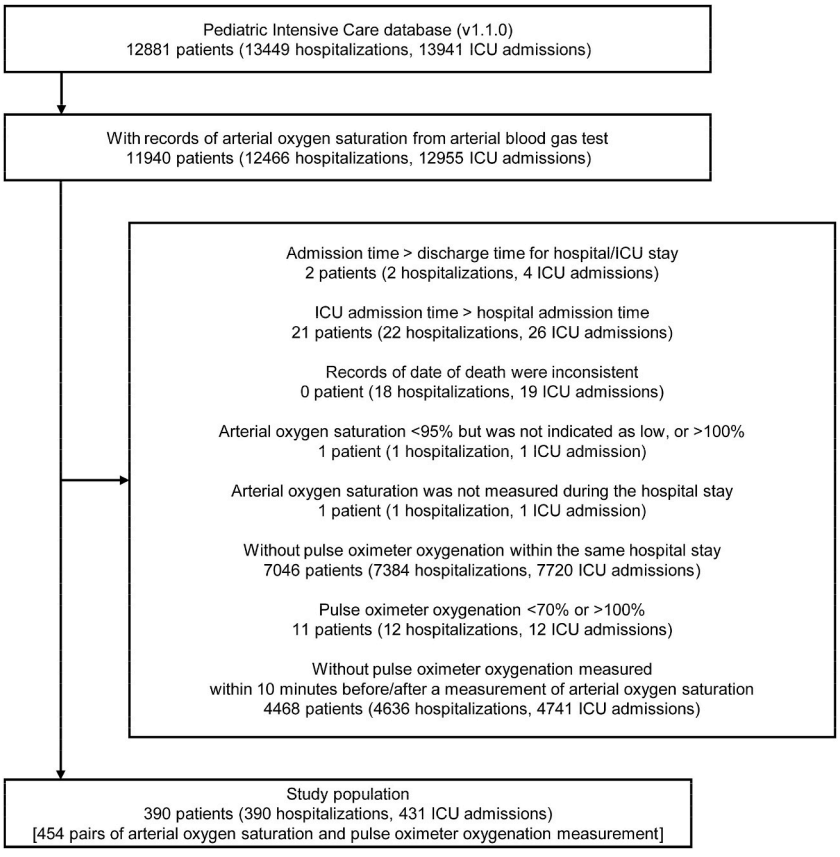

Fig. 1. Flow diagram of including the study population
Abbreviation: ICU, intensive care unit.

2.2. Study population

The study was based on a cohort study design, in which we retrospectively included all pediatric patients in the database who had ≥1 pair of records of SaO_2 and SpO_2 measured within 10 min. For data quality, we excluded a few records with inconsistent information or potential data errors. A detailed flow diagram of including the study population is presented in Fig. 1.

2.3. SaO_2, SpO_2, and occult hypoxemia

For each SaO_2-SpO_2 measurement pair, we calculated the time interval of the paired measurement (which was always <10 min by study design). To examine discrepancy between SaO_2 and SpO_2, we defined occult hypoxemia as SaO_2 <88% with the paired SpO_2 ≥92% as previously reported [26]. Since a patient might have more than one SaO_2-SpO_2 measurement pair, number of SaO_2-SpO_2 measurement pairs per patient during the same hospitalization was calculated; at the level of SaO_2-SpO_2 measurement pairs, we categorized each measurement pair as with or without occult hypoxemia; at the level of patients (i.e., at individual level), if at least one of the SaO_2-SpO_2 measurement pairs of a unique patient within the same hospitalization met the criteria of occult hypoxemia, the patient within the hospitalization would be categorized as a patient with occult hypoxemia.

2.4. Predictors/covariates

From the database, we identified the below variables as predictors or covariates for further analyses (see below Statistical analysis): 1) age on hospital admission, sex, and ethnicity; 2) admission department, (first) admitted ICU; 3) diagnoses registered during the hospitalization, including tumor or space occupying lesion, respiratory tract infection, other infection, neonatal disease, congenital heart disease, other congenital disease, shock heart failure multiple organ failure, other respiratory cardiovascular disease, digestive disease, fracture, traumatic injury, nervous system disease, and others; 4) vital signs/other lab examinations (than SaO_2 and SpO_2), including body temperature, respiratory rate, heart rate, systolic blood pressure, diastolic blood pressure, hemoglobin, and lactate; 5) surgery, and types of surgery.

The vital signs/other lab examinations were obtained from available data within 72 h before each pair of SaO_2-SpO_2 measurement but not earlier than hospital admission. If there were more than one available record, we extracted the most recent one. The same identification strategy applied to the extraction of surgical records. When summarizing vital signs/other lab examinations at individual level, we further identified the minimum and maximum record of the same patient during a hospitalization.

2.5. Clinical outcomes

In-ICU mortality and in-hospital mortality were identified from the database as clinical outcomes. We did not distinguish whether a SaO_2-SpO_2 measurement was measured within an ICU hospitalization or not, and hence the same patient during the same hospitalization would always share the same in-ICU mortality for all available SaO_2-SpO_2 measurement pairs.

2.6. Statistical analysis

Summary statistics were presented as mean ± standard deviation or median (25–75% percentiles) for continuous variables, and frequency (percentage) for categorical variables. Comparisons between two groups were examined by *t*-test or the Mann-Whitney *U* test for continuous variables, and by the Chi-squared test or the Fisher's exact test for categorical variables. We first compared the various covariates according to presence of occult hypoxemia at individual level and at the level of SaO_2-SpO_2 measurement pairs. To examine discrepancy between SaO_2 and SpO_2, we plotted the distribution of SaO_2 by SpO_2, and calculated cumulative incidence of occult hypoxemia by levels of SpO_2, with estimating 95% confidence interval (CI) by the Clopper-Pearson method. Potential predictors of occult hypoxemia were then explored by univariable logistic regression, but this was only performed at the level of SaO_2-SpO_2 measurement pairs. Last, at individual level we examined the associations between occult hypoxemia and the clinical outcomes by logistic regression with a model adjusting for age on hospital admission, sex, admission department, first admitted ICU, and diagnoses. We performed complete case analysis when there was missing value (mainly for vital signs/other lab examinations). A P-value <0.05 was considered to indicate statistical significance. IBM SPSS Statistics for Windows (version 29.0. Armonk, NY: IBM Corp.) and the R program (version 4.2.2) were used for the statistical analyses.

3. Results

3.1. General characteristics of the study population

A total of 390 patients were included with 454 pairs of SaO_2-SpO_2 readings (Fig. 1). The mean number of SaO_2-SpO_2 measurement pairs was 1.2 ± 0.6 pairs per patient, with a mean interval of SaO_2-SpO_2 measurement of 4.8 ± 2.9 min. The study population mainly consisted of Han Chinese (99.0%), with a median age of 8.2 months (25th-75th percentile 0.9–42.7 months), of which 43.6% were female. The most frequent admission departments were Burn/Neurosurgery/Neurology/Orthopedics/Traumatology department (26.2%) and neonatal ICU (NICU, 24.6%). Regarding the (first) admitted ICU, surgical ICU (SICU, 51.3%) and NICU (26.2%) were the most frequent. Regarding diagnoses, tumor or space occupying lesion (18.5%), other congenital disease (16.9%), and respiratory tract

Table 1
Baseline characteristics of the study population at individual level.

Variable	Overall (n = 390)	Occult hypoxemia		P value
		No (n = 312)	Yes (n = 78)	
Age on hospital admission				
(Months)	8.2 (0.9–42.7)	9.2 (0.9–49.0)	6.7 (1.3–27.6)	0.324
(Years)	0.7 (0.1–3.6)	0.8 (0.1–4.1)	0.6 (0.1–2.3)	0.324
Age group				0.073
0–6 months	172 (44.1)	134 (42.9)	38 (48.7)	
6 months–3 years	108 (27.7)	82 (26.3)	26 (33.3)	
3 years–18 years	110 (28.2)	96 (30.8)	14 (17.9)	
Sex				0.251
Male	220 (56.4)	181 (58.0)	39 (50.0)	
Female	170 (43.6)	131 (42.0)	39 (50.0)	
Ethnicity				0.706
Han	386 (99.0)	308 (98.7)	78 (100)	
Others	4 (1.0)	4 (1.3)	0 (0)	
Admission department				0.008
NICU	96 (24.6)	77 (24.7)	19 (24.4)	
PICU	54 (13.8)	32 (10.3)	22 (28.2)	
General ICU	11 (2.8)	10 (3.2)	1 (1.3)	
SICU	17 (4.4)	15 (4.8)	2 (2.6)	
CICU	5 (1.3)	4 (1.3)	1 (1.3)	
Cardiac surgery department	17 (4.4)	11 (3.5)	6 (7.7)	
Burn/Neurosurgery/Neurology/Orthopedics/Traumatology department	102 (26.2)	86 (27.6)	16 (20.5)	
General surgery/Neonatology surgery/Endoscopy department	48 (12.3)	43 (13.8)	5 (6.4)	
Thoracic surgery/Oncology department	32 (8.2)	27 (8.7)	5 (6.4)	
Neonatology department	4 (1.0)	4 (1.3)	0 (0.0)	
Others	4 (1.0)	3 (1.0)	1 (1.3)	
First admitted ICU				<0.001
NICU	102 (26.2)	83 (26.6)	19 (24.4)	
SICU	200 (51.3)	173 (55.4)	27 (34.6)	
CICU	23 (5.9)	14 (4.5)	9 (11.5)	
General ICU	11 (2.8)	10 (3.2)	1 (1.3)	
PICU	54 (13.8)	32 (10.3)	22 (28.2)	
Diagnoses				
Tumor or space occupying lesion	72 (18.5)	63 (20.2)	9 (11.5)	0.110
Respiratory tract infection	57 (14.6)	41 (13.1)	16 (20.5)	0.142
Other infection	29 (7.4)	24 (7.7)	5 (6.4)	0.885
Neonatal disease	53 (13.6)	43 (13.8)	10 (12.8)	0.971
Congenital heart disease	29 (7.4)	21 (6.7)	8 (10.3)	0.412
Other congenital disease	66 (16.9)	51 (16.3)	15 (19.2)	0.661
Shock heart failure multiple organ failure	13 (3.3)	10 (3.2)	3 (3.8)	1.000
Other respiratory cardiovascular disease	17 (4.4)	13 (4.2)	4 (5.1)	0.951
Digestive disease	52 (13.3)	45 (14.4)	7 (9.0)	0.280
Fracture	12 (3.1)	11 (3.5)	1 (1.3)	0.509
Traumatic injury	28 (7.2)	22 (7.1)	6 (7.7)	1.000
Nervous system disease	42 (10.8)	33 (10.6)	9 (11.5)	0.967
Others	32 (8.2)	23 (7.4)	9 (11.5)	0.333
Number of SaO_2-SpO_2 measurement pairs	1.2 ± 0.6	1.1 ± 0.3	1.4 ± 1.0	<0.001
Time interval of paired SaO_2-SpO_2 measurement (min)				
Min	4.6 ± 2.9	4.8 ± 2.9	4.0 ± 2.9	0.025
Max	5.1 ± 3.0	5.1 ± 3.0	5.1 ± 3.0	0.983
SaO_2 (%)				
Min	91.9 ± 13.7	97.0 ± 6.3	71.4 ± 15.8	<0.001
Max	93.3 ± 12.4	97.5 ± 5.0	76.7 ± 18.2	<0.001
SpO_2 (%)				
Min	97.8 ± 4.5	97.9 ± 4.5	97.2 ± 4.5	0.180
Max	98.2 ± 3.9	98.2 ± 4.2	98.4 ± 2.2	0.670
Vital signs/Other lab examinations				
Body temperature (°C)				
Min	36.7 ± 0.8	36.7 ± 0.8	36.8 ± 0.7	0.328
Max	36.8 ± 0.8	36.7 ± 0.8	36.9 ± 0.8	0.040
Respiratory rate (/min)				
Min	38.2 ± 16.7	37.5 ± 16.8	41.0 ± 16.1	0.103
Max	39.3 ± 17.6	38.2 ± 17.4	43.3 ± 17.9	0.022
Heart rate (bpm)				
Min	123.0 ± 23.2	121.4 ± 22.3	129.9 ± 25.9	0.025
Max	123.4 ± 23.4	121.6 ± 22.5	131.3 ± 25.7	0.012
Systolic blood pressure (mmHg)				
Min	97.1 ± 23.8	98.1 ± 24.4	93.5 ± 21.1	0.176

(*continued on next page*)

Table 1 (*continued*)

Variable	Overall (n = 390)	Occult hypoxemia		P value
		No (n = 312)	Yes (n = 78)	
Max	98.1 ± 23.2	98.8 ± 23.8	95.8 ± 20.9	0.361
Diastolic blood pressure				
Min	56.7 ± 18.1	57.6 ± 18.6	53.5 ± 15.7	0.110
Max	57.5 ± 17.6	58.2 ± 18.2	55.3 ± 15.4	0.249
Hemoglobin (g/dL)				
Min	95.0 ± 44.3	95.3 ± 44.2	94.1 ± 45.0	0.848
Max	96.3 ± 45.0	96.0 ± 44.6	97.7 ± 47.4	0.785
Lactate (mmol/L)				
Min	2.5 ± 2.4	2.4 ± 2.5	2.6 ± 2.4	0.574
Max	2.6 ± 2.6	2.5 ± 2.5	3.1 ± 2.6	0.126
Surgery	172 (44.1)	147 (47.1)	25 (32.1)	0.023
Length of hospital stay (days)	13.2 (7.1–22.0)	13.2 (7.0–21.2)	13.3 (8.4–24.9)	0.412

The category "Others" of Admission department refers to Pediatric internal medicine, Respiratory medicine department, Cardiovascular department, Gastroenterology department, Hematology department, Ophthalmology department/ENT, Infectious diseases department, Endocrinology department, Rheumatology department, or Nephrology department.
Abbreviations: NICU: neonatal intensive care unit; PICU: pediatric intensive care unit; ICU: intensive care unit; SICU: surgical intensive care unit; CICU: cardiac intensive care unit.

infection (14.6%) were the most frequent. Other patient characteristics are shown in Table 1.

3.2. Occult hypoxemia by levels of SpO_2

Occult hypoxemia was observed in 20.0% (78/390, 95%CI 16.1–24.3%) of the patients (corresponding to 18.9% [86/454, 95%CI 15.4–22.9%] of the measurement pairs, Table 2), with a mean SaO_2 of 71.4 ± 15.8% and SpO_2 of 97.2 ± 4.5% (Table 1). Patients with occult hypoxemia had significantly greater number of SaO_2-SpO_2 measurement pairs than those without occult hypoxemia (1.4 ± 1.0 versus 1.1 ± 0.3, $P < 0.001$), and the (minimum) time interval of paired SaO_2-SpO_2 measurement was also shorter (4.0 ± 2.9 versus 4.8 ± 2.9 min, $P = 0.025$). The distribution of SaO2 by SpO2 is presented in Fig. 2-A, and there seemed a decreasing trend of occult hypoxemia with the increase of SpO2 (Fig. 2-B).

3.3. Predictors of occult hypoxemia

As shown in Table 3, potential predictors of occult hypoxemia included female (OR = 1.53, 95%CI 0.95–2.46), being first admitted to cardiac ICU (OR = 3.68, 95%CI 1.68–7.88), congenital heart disease (OR = 2.05, 95%CI 0.96–4.15), increased heart rate (OR = 1.01 per 1 bpm increase, 95%CI 1.00–1.03), while patients with prior surgery records were less likely to experience occult hypoxemia (OR = 0.56, 95%CI 0.33–0.93). These findings were generally in line with the comparison of patient characteristics by presence of occult hypoxemia shown in Tables 1 and 2

3.4. Associations of occult hypoxemia with clinical outcomes

Patients with occult hypoxemia had numerically higher in-ICU mortality rate (16.7%) than those without occult hypoxemia (10.9%), but the difference was not statistically significant (adjusted OR = 0.94, 95%CI 0.39–2.19). Similar result was observed for in-hospital mortality in Table 4 (17.9% versus 10.9%, adjusted OR = 1.10, 95%CI 0.46–2.52).

4. Discussion

In the current study we examined potential discrepancy between SaO_2 and SpO_2 measurement in a Chinese pediatric patient cohort who had ICU admission during hospitalizations. Our main findings were 1) incidence of occult hypoxemia was substantial (i.e., 20%) among the investigated pediatric patient cohort; 2) occult hypoxemia seemed more likely to present when SpO_2 reading was relatively lower; 3) female sex, cardiac ICU admission, congenital heart disease, and increased heart rate might help predict occult hypoxemia; 4) occult hypoxemia appeared to associate with increased mortality. Given that there were no studies that had included an Asian pediatric population regarding accuracy of pulse oximetry measurement, our study helps fill in the knowledge gap. Since the incidence of occult hypoxemia was rather high and it seemed to associate with worse survival, clinicians should be aware of this and should not rely on pulse oximetry measurement only for monitoring hypoxemia. The several predictors we reported could be helpful for identifying Chinese pediatric ICU patients at risk of occult hypoxemia. What we found also suggests the racial bias of pulse oximetry measurement consistently applies to other race/ethnicity (than Black people), and hence they should not be ignored in relevant research.

The COVID-19 pandemic, to some extent, further attracted attention into racial bias of pulse oximetry measurement since it was widely used to identify high-risk COVID-19 patients [1]. According to a recent meta-analysis [27], a higher level of skin pigmentation (or Black/African American) was associated with overestimated oxygen saturation, but this association was uncertain in other ethnic groups. The incidence of occult hypoxemia we observed in the Chinese pediatric population (20.0%, 95%CI 16.1–24.3%) was between

Table 2
Baseline characteristics of the study population at the level of SaO_2-SpO_2 measurement pairs.

Variable	Overall (n = 454)	Occult hypoxemia		P value
		No (n = 368)	Yes (n = 86)	
Age on hospital admission				
(Months)	6.3 (0.4–37.2)	6.3 (0.2–40.9)	6.2 (0.7–20.9)	0.779
(Years)	0.5 (0.0–3.1)	0.5 (0.0–3.4)	0.5 (0.1–1.7)	0.779
Age group				0.125
0–6 months	221 (48.7)	178 (48.4)	43 (50.0)	
6 months–3 years	119 (26.2)	91 (24.7)	28 (32.6)	
3 years–18 years	114 (25.1)	99 (26.9)	15 (17.4)	
Sex				0.099
Male	250 (55.1)	210 (57.1)	40 (46.5)	
Female	204 (44.9)	158 (42.9)	46 (53.5)	
Ethnicity				0.741
Han	450 (99.1)	364 (98.9)	86 (100)	
Others	4 (0.9)	4 (1.1)	0 (0)	
Admission department				0.007
NICU	133 (29.3)	113 (30.7)	20 (23.3)	
PICU	66 (14.5)	43 (11.7)	23 (26.7)	
General ICU	13 (2.9)	12 (3.3)	1 (1.2)	
SICU	18 (4.0)	15 (4.1)	3 (3.5)	
CICU	12 (2.6)	7 (1.9)	5 (5.8)	
Cardiac surgery department	17 (3.7)	11 (3.0)	6 (7.0)	
Burn/Neurosurgery/Neurology/Orthopedics/Traumatology department	105 (23.1)	88 (23.9)	17 (19.8)	
General surgery/Neonatology surgery/Endoscopy department	48 (10.6)	43 (11.7)	5 (5.8)	
Thoracic surgery/Oncology department	33 (7.3)	28 (7.6)	5 (5.8)	
Neonatology department	4 (0.9)	4 (1.1)	0 (0.0)	
Others	5 (1.1)	4 (1.1)	1 (1.2)	
First admitted ICU				<0.001
NICU	139 (30.6)	119 (32.3)	20 (23.3)	
SICU	205 (45.2)	176 (47.8)	29 (33.7)	
CICU	30 (6.6)	17 (4.6)	13 (15.1)	
General ICU	13 (2.9)	12 (3.3)	1 (1.2)	
PICU	67 (14.8)	44 (12.0)	23 (26.7)	
Diagnoses				
Tumor or space occupying lesion	75 (16.5)	65 (17.7)	10 (11.6)	0.232
Respiratory tract infection	69 (15.2)	53 (14.4)	16 (18.6)	0.418
Other infection	32 (7.0)	27 (7.3)	5 (5.8)	0.793
Neonatal disease	70 (15.4)	60 (16.3)	10 (11.6)	0.360
Congenital heart disease	39 (8.6)	27 (7.3)	12 (14.0)	0.079
Other congenital disease	78 (17.2)	62 (16.8)	16 (18.6)	0.818
Shock heart failure multiple organ failure	17 (3.7)	14 (3.8)	3 (3.5)	1.000
Other respiratory cardiovascular disease	22 (4.8)	18 (4.9)	4 (4.7)	1.000
Digestive disease	58 (12.8)	51 (13.9)	7 (8.1)	0.211
Fracture	12 (2.6)	11 (3.0)	1 (1.2)	0.564
Traumatic injury	31 (6.8)	25 (6.8)	6 (7.0)	1.000
Nervous system disease	48 (10.6)	38 (10.3)	10 (11.6)	0.874
Others	38 (8.4)	28 (7.6)	10 (11.6)	0.320
Time interval of paired SaO_2-SpO_2 measurement (min)	4.8 ± 2.9	4.9 ± 2.9	4.4 ± 3.0	0.110
SaO_2 (%)	92.3 ± 13.1	96.9 ± 6.9	72.8 ± 15.2	<0.001
SpO_2 (%)	97.7 ± 4.6	97.6 ± 5.0	98.1 ± 2.5	0.373
Vital signs/Other lab examinations				
Body temperature (°C)	36.8 ± 0.8	36.7 ± 0.8	36.9 ± 0.8	0.128
Respiratory rate (/min)	40.6 ± 17.1	40.0 ± 17.2	42.7 ± 16.5	0.199
Heart rate (bpm)	125.2 ± 23.2	124.1 ± 22.5	130.3 ± 25.5	0.077
Systolic blood pressure (mmHg)	94.6 ± 24.0	94.9 ± 24.8	93.4 ± 21.3	0.627
Diastolic blood pressure	55.1 ± 17.9	55.4 ± 18.6	53.8 ± 14.9	0.495
Hemoglobin (g/dL)	96.1 ± 47.2	96.2 ± 47.0	95.9 ± 47.9	0.956
Lactate (mmol/L)	2.7 ± 2.5	2.6 ± 2.6	2.8 ± 2.3	0.631
Surgery	174 (38.3)	150 (40.8)	24 (27.9)	0.037
Surgery type				0.181
No surgery	280 (61.7)	218 (59.2)	62 (72.1)	
Surgery for brain/spine	64 (14.1)	54 (14.7)	10 (11.6)	
Thoracic/cardiac surgery	13 (2.9)	10 (2.7)	3 (3.5)	
Abdominal/pelvic surgery	74 (16.3)	65 (17.7)	9 (10.5)	
Other surgery	23 (5.1)	21 (5.7)	2 (2.3)	

The category "Others" of Admission department refers to Pediatric internal medicine, Respiratory medicine department, Cardiovascular department, Gastroenterology department, Hematology department, Ophthalmology department/ENT, Infectious diseases department, Endocrinology department, Rheumatology department, or Nephrology department.

Abbreviations: NICU: neonatal intensive care unit; PICU: pediatric intensive care unit; ICU: intensive care unit; SICU: surgical intensive care unit; CICU: cardiac intensive care unit.

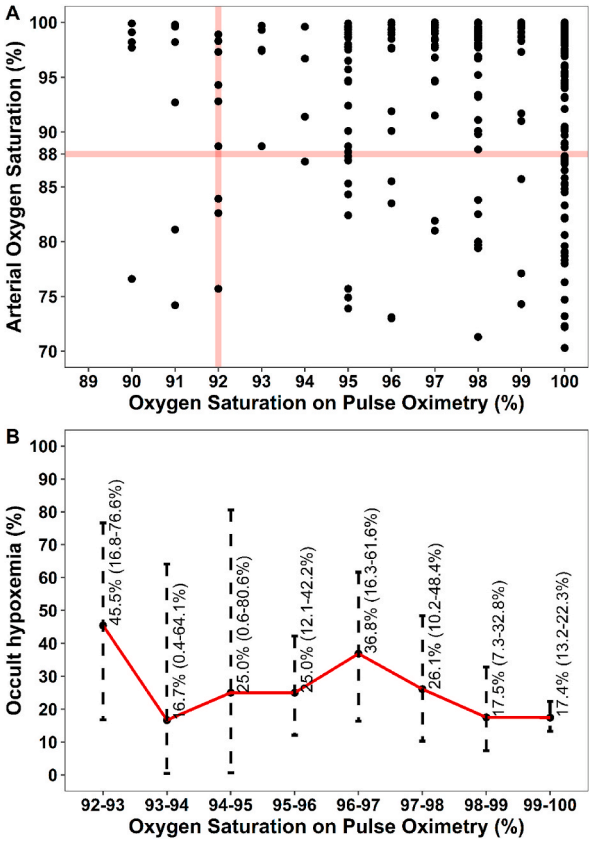

Fig. 2. Accuracy of pulse oximetry in measuring arterial oxygen saturation
Occult hypoxemia was defined as SaO_2 <88% with the paired SpO_2 ≥92%.
A: the distribution of SaO2 by SpO2; B: proportion of occult hypoxemia by levels of SpO2, where occult hypoxemia was defined as SaO2 <88% with the paired SpO2 ≥92%.

that observed in the White patients (15.6%, 95%CI 13.3%–18.2%) and in the Black patients (21.1%, 95%CI 15.7%–27.7%) [21]. There are, however, variations in the reported incidence of occult hypoxemia between studies, which might be explained by difference in study populations and definitions of occult hypoxemia [22–24]. We found the incidence of occult hypoxemia seemed lower when the reading of SpO_2 was relatively higher, and this is consistent with the study by Chesley et al. [8], in which occult hypoxemia was found to reduce at oxygenation saturation range 95–100%. In the study we also explored potential predictors of occult hypoxemia as well as its association with clinical outcomes, which was rarely performed in other pediatric studies. We found patients who were admitted to cardiac ICU admission, who had congenital heart disease, or those with increased heart rate appeared to associate with increased risk of occult hypoxemia. To some extent, this was in line with the findings that patients with tricuspid regurgitation had greater discrepancies between SaO_2 and SpO_2 [28]. Female sex seems also a risk factor, and consistently, in the study by Burnett et al. [29], male patients tended to have lower odds of occult hypoxemia than female patients (OR = 0.89, 95%CI 0.75–1.06). These results should be interpreted with cautions, as we did not find statistically significant associations (which might be due to the small sample size) and there were not similar investigations so far in pediatric populations. Regarding the association between occult hypoxemia and clinical outcomes, we found patients with occult hypoxemia had numerically higher (but not statistically significant) risk of (in-hospital and in-ICU) mortality. The study by Savorgnan et al. [30] was the only one study that included pediatric population and reported the association between occult hypoxemia and clinical outcome, but they found no difference in length of hospital stay after controlling levels of support. Again, our findings should be carefully interpreted. Due to the lack of a control cohort and treatment information, it is unknown whether the higher mortality rate was truly related to occult hypoxemia and the SaO_2-SpO_2 discrepancy. Other sources of bias might also challenge our comparison of clinical outcomes between patients with and without occult hypoxemia. Since the patients with occult hypoxemia received more frequent oxygen measurement, it was likely that they showed other signs of hypoxemia and hence received more medical attention and more intensive care, which might bias the association toward null. The direction of bias could be also in the opposite direction, as patients with occult hypoxemia might be already under a severer condition and hence they

Table 3
Associations of baseline characteristics with occult hypoxemia (based on univariable analysis).

Variable	No. SaO_2-SpO_2 measurement pair	Occult hypoxemia	OR (95% CI)	P value
Age on hospital admission				
(Months)	454	86 (18.9)	1.00 (0.99–1.00)	0.294
(Years)	454	86 (18.9)	0.96 (0.88–1.03)	0.294
Age group				
0–6 months	221	43 (19.5)	1 (Reference)	–
6 months–3 years	119	28 (23.5)	1.27 (0.74–2.17)	0.379
3 years–18 years	114	15 (13.2)	0.63 (0.32–1.16)	0.151
Sex				
Male	250	40 (16.0)	1 (Reference)	–
Female	204	46 (22.5)	1.53 (0.95–2.46)	0.078
Ethnicity				
Han	450	86 (19.1)	1 (Reference)	–
Others	4	0 (0)	–	–
First admitted ICU				
Other ICUs	424	73 (17.2)	1 (Reference)	–
CICU	30	13 (43.3)	3.68 (1.68–7.88)	<0.001
Diagnoses (versus those without the diagnosis)				
Tumor or space occupying lesion	75	10 (13.3)	0.61 (0.29–1.20)	0.178
Respiratory tract infection	69	16 (23.2)	1.36 (0.72–2.47)	0.330
Other infection	32	5 (15.6)	0.78 (0.26–1.93)	0.620
Neonatal disease	70	10 (14.3)	0.68 (0.31–1.33)	0.282
Congenital heart disease	39	12 (30.8)	2.05 (0.96–4.15)	0.053
Other congenital disease	78	16 (20.5)	1.13 (0.60–2.03)	0.698
Shock heart failure multiple organ failure	17	3 (17.6)	0.91 (0.21–2.88)	0.890
Other respiratory cardiovascular disease	22	4 (18.2)	0.95 (0.27–2.62)	0.926
Digestive disease	58	7 (12.1)	0.55 (0.22–1.19)	0.158
Fracture	12	1 (8.3)	0.38 (0.02–2.00)	0.360
Traumatic injury	31	6 (19.4)	1.03 (0.37–2.44)	0.952
Nervous system disease	48	10 (20.8)	1.14 (0.52–2.31)	0.724
Others	38	10 (26.3)	1.60 (0.71–3.33)	0.229
Vital signs/Other lab examinations				
Body temperature (°C)	436	85 (19.5)	1.27 (0.94–1.72)	0.128
Respiratory rate (/min)	437	86 (19.7)	1.01 (1.00–1.02)	0.200
Heart rate (bpm)	291	54 (18.6)	1.01 (1.00–1.03)	0.078
Systolic blood pressure (mmHg)	355	75 (21.1)	1.00 (0.99–1.01)	0.626
Diastolic blood pressure	355	75 (21.1)	0.99 (0.98–1.01)	0.494
Hemoglobin (g/dL)	406	77 (19.0)	1.00 (0.99–1.01)	0.956
Lactate (mmol/L)	405	76 (18.8)	1.02 (0.92–1.12)	0.631
Surgery				
No	280	62 (22.1)	1 (Reference)	–
Yes	174	24 (13.8)	0.56 (0.33–0.93)	0.029

Abbreviations: OR, odds ratio; CI, confidence interval; ICU: intensive care unit; CICU: cardiac intensive care unit.

Table 4
Associations of occult hypoxemia with clinical outcomes.

Variable	No. Patients	Summary statistics of outcome	Crude OR (95% CI)	P value	Adjusted OR (95%CI)	P value
In-ICU mortality						
Occult hypoxemia						
No	312	34 (10.9)	1 (Reference)	–	1 (Reference)	–
Yes	78	13 (16.7)	1.64 (0.79–3.21)	0.165	0.94 (0.39–2.19)	0.890
In-hospital mortality						
Occult hypoxemia						
No	312	34 (10.9)	1 (Reference)	–	1 (Reference)	–
Yes	78	14 (17.9)	1.79 (0.88–3.47)	0.093	1.10 (0.46–2.52)	0.828

The adjusted OR was adjusted for age on hospital admission (months), sex, admission department, first admitted ICU, tumor or space occupying lesion, respiratory tract infection, other infection, neonatal disease, congenital heart disease, other congenital disease, shock heart failure multiple organ failure, other respiratory cardiovascular disease, digestive disease, fracture, traumatic injury, nervous system disease, and other diagnoses.
Abbreviations: OR, odds ratio; CI, confidence interval; ICU: intensive care unit.

were measured more frequently, which explained the observed worse survival, instead of occult hypoxemia.

Our study is with some limitations. First, similar to most of the other studies, we did not have information about skin pigmentation, and we assumed the Chinese ethnicity (mainly Han Chinese in our study) as a single level of skin pigmentation. This seems acceptable as in general the degree of skin pigmentation of Chinese people should be between Black people and White people. However, there are

still variations in skin pigmentation among Chinese people, which we were unable to consider. In addition, diseases/conditions such as jaundice and cyanotic heart disease might also affect skin color, and hence quantification of skin pigmentation no doubt will be the ideal exposure to investigate regarding its association with accuracy of pulse oximetry measurement. There is more than one way of measuring SaO_2 and SpO_2, but the technical details about the measurement methods as well as data quality for the data we had accessed to are unavailable, so our findings might not apply to settings when other measurement methods of SaO_2/SpO_2 are used. Second, the sample size in our study was actually limited, and most of the predictors of occult hypoxemia we identified as well as the association between occult hypoxemia and mortality were not statistically significant (though the 95%CIs were toward the direction with increased risk). Similarly, our investigation into the associations between occult hypoxemia and clinical outcomes could be underpowered. This means our findings need to be confirmed in future studies with larger sample sizes. Third, due to the nature of retrospective study design, selection bias cannot be ruled out because only patients who had records of both SaO_2 and SpO_2 measured within 10 min would be included into our study. As mentioned above, it is likely that patients with higher risk of occult hypoxemia would receive more frequent/intensive oxygen measurement and therefore were more likely to be included into our study. It was also uncertain how reliable the recorded timing of a measurement was. To address these limitations, a prospective study design with detailed treatment information is warranted. Last but not least, there are many other factors which might affect the accuracy of pulse oximetry but were not considered in our study [2]. For newborns, fetal hemoglobin is another factor that might bias SaO_2, which should be considered in future studies if data are available. It would also be interesting to further explore whether the observed SaO_2-SpO_2 discrepancy differs between patient subgroups, which also requires a larger sample size.

5. Conclusion

There was a substantial proportion of hypoxemia that was not detected by pulse oximetry in the investigated Chinese pediatric patients, which might be predicted by several patient characteristics and seemed to associate with mortality.

Data availability statement

The study used data from the Pediatric Intensive Care (PIC) database (version 1.1.0) which cannot be directly shared by the authors according to the data use agreement, however, access to the data is possible after following the required application procedures of the database (http://pic.nbscn.org/applyhome).

Ethics declarations

This study was reviewed and approved by the Institutional Review Board of the Guangdong Provincial People's Hospital, with the approval number KY2023-225. Informed consent was not required for this study because the project did not impact clinical care, and all protected health information was deidentified.

CRediT authorship contribution statement

Qin-chang Chen: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Jun–jun Shen:** Writing – review & editing, Data curation. **Yu-lu Huang:** Writing – review & editing, Data curation. **Ran Kong:** Writing – review & editing. **Yu-mei Xie:** Writing – review & editing. **Shu-shui Wang:** Writing – review & editing, Project administration, Methodology.

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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