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Correlation of radiographic thoracic area and oxygenation impairment in bronchopulmonary dysplasia

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ABSTRACT

We hypothesized that radiographically-assessed hyperinflation in bronchopulmonary dysplasia (BPD) is related to the degree of oxygenation impairment. Our objective was to explore the relation of chest radiographic thoracic area (CRTA) with right-to-left shunt, right shift of the oxyhemoglobin dissociation curve and ventilation/perfusion ratio (V_A/Q) in infants with BPD. Twenty-two infants born at median (IQR) gestation of 26 (24–28) weeks with BPD were prospectively studied at 39 (30–69) days. Inspired oxygen (FiO_2) was varied to obtain transcutaneous oxygen saturation (SpO_2) values between 85 and 96%. Shunt, shift and V_A/Q were derived by plotting and analysing pairs of SpO_2 and FiO_2. CRTA was measured by free hand-tracing the perimeter of the thoracic area in anterio–posterior chest radiographs. Median (IQR) shunt was 8 (1–14)%, shift was 13 (11–19) kPa and V_A/Q 0.42 (0.30–0.48). Median (IQR) CRTA/kg was 2495 (1962–2838) mm^2 and was significantly related to shift ($r = 0.674$, $p < 0.001$), V_A/Q ($r = -0.633$, $p < 0.001$), weight at study ($r = -0.457$, $p = 0.003$) and day of life ($r = -0.406$, $p = 0.009$), but not to shunt. CRTA in BPD is significantly related to oxygenation impairment as quantified by shift and V_A/Q. CRTA can be used as a simple radiographic test to quantify BPD severity.

1. Introduction

Bronchopulmonary dysplasia (BPD) is a frequent adverse outcome of extreme premature birth and is associated with significant respiratory morbidity (Jensen and Schmidt, 2014). The radiographic appearance of BPD has evolved over the years and is currently characterised by interstitial fibrosis and hyperinflation (Greenough et al., 2000). Hyperinflation is a cardinal radiologic finding in BPD and reflects distorted lung architecture and ventilation inhomogeneity. Hyperinflation can be assessed with the estimation of the functional residual capacity (FRC) by plethysmography (Beydon et al., 2007). Unfortunately, this method involves complex methodology and equipment, which is not readily available in most neonatal units caring for infants with BPD. Alternatively, the estimation of the chest radiograph thoracic area (CRTA) has been proposed as a simple reliable radiographic method to assess hyperinflation (Dimitriou et al., 1999). A good correlation between CRTA and FRC by helium dilution and minimal intra- and inter-observer variability have been reported (May et al., 2009).

Oxygenation impairment is an important pathophysiological marker of BPD. The level of supplemental oxygen required to overcome this impairment is widely used as an index to stratify BPD into categories of severity (Jobe and Bancalari, 2001). Oxygenation impairment in BPD can be non-invasively quantified in a continuous spectrum by measurements of: the degree of the right to left shunt (shunt), i.e. the amount of deoxygenated blood entering the systemic circulation without undergoing any alveolar gas-exchange; the degree of right shift of the oxyhemoglobin dissociation curve (shift); and the degree of reduction in the ventilation to perfusion ratio (V_A/Q) (Quine et al., 2006). Shunt, shift and V_A/Q can all be measured non-invasively and used to quantify disease severity in BPD. The relative effect of shunt, shift and V_A/Q on oxygenation impairment can be visualised by plotting arterial oxygen saturation versus the pressure of inspired oxygen (PiO_2). In concept, the degree of depression of the curve downwards quantifies the level of right to left shunt whereas decreasing V_A/Q "shifts" the curve to the right (Fig. 1) (Roe and Jones, 1993; Sapsford and Jones, 1995).

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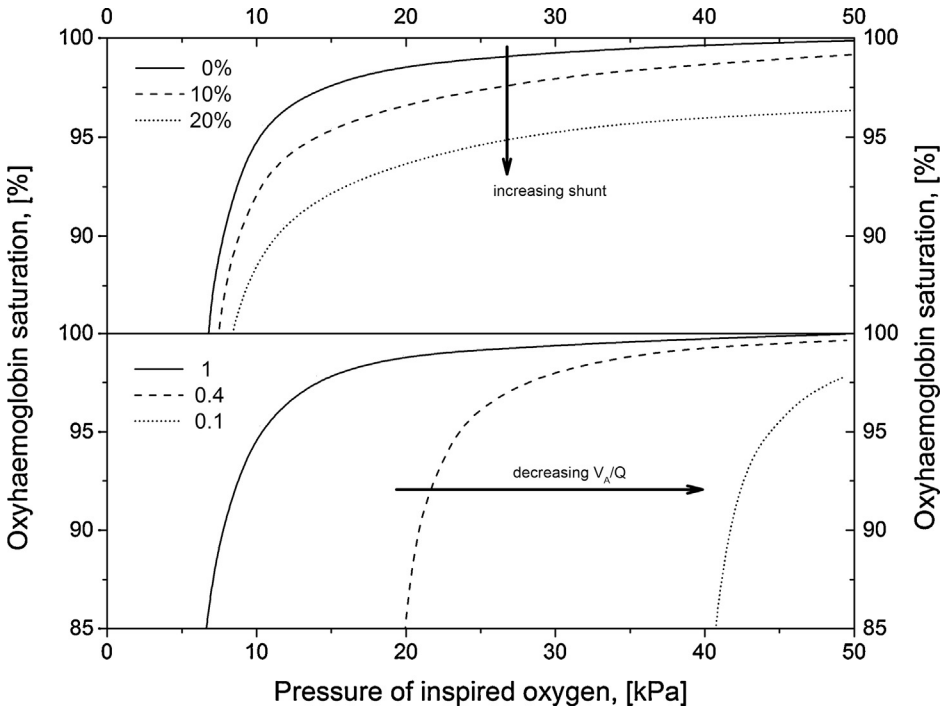

Fig. 1. The oxygen hemoglobin dissociation curve: proportion of hemoglobin saturation versus pressure of inspired oxygen. Increasing shunt from 0% to 10% and 20% (upper diagram) displaces the curve downwards and decreasing V_A/Q (lower diagram) shifts the curve to the right. This is a graphic representation of the concept from non-infant data.

Inhomogeneities of ventilation and perfusion are common in BPD and result in alveolar dead space that increases the total ventilation required to maintain eucapnia. Relatively under-ventilated regions of the lungs cause alveolar hypoxia and hypoxemia (Loring et al., 2009).

We hypothesised that hyperinflation in BPD would be significantly associated with the degree of oxygenation impairment. Our objective was thus to examine the relation of CRTA with shunt, shift and V_A/Q in infants with BPD and explore the possible utility of CRTA as a simple radiographic index of BPD severity.

2. Material and methods

2.1. Subjects

Infants born <32 weeks gestation treated with oxygen at 28 days after birth were eligible. Postmenstrual age (PMA) was calculated in weeks as the sum of gestational age plus chronological age at the time of measurement (for example an infant born at 28 weeks of gestation studied at 6 weeks of life, would have a postmenstrual age of 34 weeks). This was a prospective study. Infants with acute atelectasis on the radiograph and infants with coexisting congenital respiratory or cardiac disorders, as well as infants with hemodynamically-significant patent ductus arteriosus (PDA) were excluded. Infants were studied in the neonatal unit of the Rosie Maternity Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK. The study was approved by the institutional research ethics committee. Written informed parental consent was obtained for each infant. All eligible infants between November 2013 and June 2014 were included.

2.2. Measurements of shunt, shift and V_A/Q

Since atmospheric pressure at sea-level is 101 kPa and oxygen content of air is 21%, the partial pressure of oxygen at sea-level is 21 kPa. Thus, percentage of FiO_2 needed to treat infants was regarded as the same value as PiO_2 in kiloPascal. Peripheral oxygen saturation (SpO_2) and FiO_2 were measured when the subjects were clinically stable and sleeping. A SpO_2 probe was attached to the right hand and the result displayed on screen. The FiO_2 was then varied in 3% increments and the SpO_2 recorded. Three–five SpO_2 levels were selected between 85% and 96% and the FiO_2 required to maintain each SpO_2, for 5 min, was recorded. This method has been applied (Dassios et al., 2015) and validated in infants with BPD (Bamat et al., 2015). A previously published computer software algorithm was used, which analyses and fits pairs of FiO_2 and SpO_2 data, produces a curve which represents the best fit of shift and shunt for each infant's data and calculates the shunt, shift and V_A/Q (Sapsford and Jones, 1995). Infants on low-flow nasal cannulae oxygen at study were measured in head-box oxygen, as inhalation of ambient air during inspiration, around the nasal cannulae, would result in a lower and unknown FiO_2 than provided. The head-box is a clear plastic hood that surrounds the infant's head and is used to provide relatively stable concentrations of warm humidified oxygen.

2.3. Chest radiographs

Anterio–posterior chest radiographs were obtained in the supine position within 48 h of shunt, shift and V_A/Q measurement for clinical purposes such as screening for possible acute infection, and nasogastric or endotracheal tube position confirmation. Infants with pneumothorax or obvious atelectasis on the chest radiograph were excluded from the study. The radiographs were obtained at end inspiration at a standard distance of 1 m above the infant as per unit protocol and imported as digital image files from the picture archiving and communicating system (PACS) (Centricity, GE Medical Systems, Barrington, IL). The software automatically adjusted for magnification errors. Free-hand tracing of the perimeter of the thoracic area as outlined by the diaphragm and the rib cage was undertaken by a consultant radiologist (MK) and the CRTA was calculated by the GE Centricity PACS software (Fig. 2). The radi-