Tidal Volume Delivery during the Anesthetic Management of Neonates Is Variable

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Objectives To describe expiratory tidal volume (V_T) during routine anesthetic management of neonates at a single tertiary neonatal surgical center, as well as the proportion of V_T values within the range of 4.0-8.0 mL/kg.

Study design A total of 26 neonates needing surgery under general anesthesia were studied, of whom 18 were intubated postoperatively. V_T was measured continuously during normal clinical care using a dedicated neonatal respiratory function monitor (RFM), with clinicians blinded to values. V_T, pressure, and cardiorespiratory variables were recorded regularly while intubated intraoperatively, during postoperative transport, and for 15 minutes after returning to the neonatal intensive care unit (NICU). In addition, paired V_T values from the anesthetic machine were documented intraoperatively.

Results A total of 2597 V_T measures were recorded from 26 neonates. Intraoperative and postoperative transport expiratory V_T values were highly variable compared with the NICU V_T ($P < .0001$, Kruskal-Wallis test), with 51% of inflations outside the 4.0-8.0 mL/kg range (35% and 38% of V_T >8.0 mL/kg, respectively), compared with 29% in the NICU ($P < .001$, χ^2 test). The use of a flow-inflating bag resulted in a median (range) V_T of 8.5 mL/kg (range, 5.3-11.4 mL/kg) vs 5.6 ml/kg (range, 4.3-7.9 mL/kg) using a Neopuff T-piece system ($P < .0001$, Mann-Whitney *U* test). The mean anesthetic machine expiratory V_T was 3.2 mL/kg (95% CI, -4.5 to 10.8 mL/kg) above RFM.

Conclusions V_T is highly variable during the anesthetic care of neonates, and potentially injurious V_T is frequently delivered; thus, we suggest close V_T monitoring using a dedicated neonatal RFM. *(J Pediatr 2017;184:51-6).*

Mechanical respiratory support alters lung mechanics and exposes the lung to the risk of injury from inappropriate tidal volumes.[1-3] Neonates are at particularly high risk for ventilator-induced lung injury (VILI) owing to their developing respiratory system and poor central respiratory control, especially if preterm.[3,4] In the diseased neonatal lung, both excessive (volutrauma) and inadequate (atelectasis) tidal volumes can cause VILI.[5,6] Lung-protective approaches, such as volume-targeted ventilation and permissive hypercapnia, aiming for a tidal volume (V_T) between 4.0 and 8.0 mL/kg, are increasingly being advocated.[7-9]

Accurate measurements of flow and volume are required to deliver V_T within a narrow range. This is challenging in neonates owing to their small size and consequent small absolute V_T.[10] Although highly accurate V_T measurements are available in the neonatal intensive care unit (NICU),[11] measurement of V_T in other clinical environments is infrequent.[12] Compounding this problem, outside of the NICU, tidal respiratory support is often provided without the aid of a mechanical ventilator and an endotracheal tube (ETT). In the delivery room, high intersubject and intrasubject variability of V_T delivery has been reported with the use of face masks and manual devices, such as self-inflating bags.[13] A more concerning finding was the frequent occurrence of high V_T volumes previously shown to cause injury in preterm lambs.[13-15]

Similar to the delivery room, anesthetic care occurs in a dynamic environment with different types of respiratory support, and lacks recommendations regarding respiratory monitoring. Anesthetic care is also often provided at different times and in different locations, such as in the operating theatre, during induction, and during intrahospital transport.

V_T delivery during the anesthetic management of neonates undergoing surgery has not been reported. We hypothesized that V_T delivery would be highly variable and frequently outside the ranges targeted in the NICU,[9] owing to a lack of direct clinical feedback and the inaccuracy of existing equipment.[13,16]

The aims of this pragmatic prospective observational noninterventional study were to describe expiratory V_T (V_{Te}) during different phases of the management

ETT	Endotracheal tube	RFM	Respiratory function monitor
FiO_2	Fraction of inspired oxygen	SpO_2	Peripheral oxyhemoglobin saturation
NICU	Neonatal intensive care unit	VILI	Ventilator-induced lung injury
PIP	Peak inflation pressure	V_T	Tidal volume
PEEP	Positive end-expiratory pressure	V_{Te}	Expiratory tidal volume

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of neonates undergoing surgery under general anesthesia, and to determine the proportion of V_{Te} values within a 4.0-8.0 mL/kg range.

Methods

The study was conducted in the operating theatre suite and NICU of the Royal Children's Hospital, Melbourne (a regional referral tertiary neonatal surgical center) between April and September 2015 in accordance with STROBE guidelines. It was approved by the hospital's Ethics in Human Research Committee, and written parental consent was obtained for each participant. Neonates aged ≤28 days (or at ≤28 days after the expected delivery date if born at <37 weeks) admitted to the NICU were considered eligible if they were scheduled to undergo any surgery under general anesthesia except cardiac surgery, and were anticipated to receive mechanical ventilation via the same ETT intraoperatively and postoperatively. Neonates were not excluded based on inotropic, analgesia, or sedative therapy or a primary respiratory diagnosis at enrollment. The type and size of the ETT and the mode of respiratory support were at the discretion of the clinical staff.

Neonates receiving high-frequency oscillatory ventilation or with a medical condition affecting the accuracy of respiratory monitoring, such as congenital cardiac disease, at enrollment were excluded. A neonate was deemed ineligible if the treating clinician believed that monitoring of V_T would impact clinical care.

V_{Te}, positive end-expiratory pressure (PEEP), and peak inspiratory pressure (PIP) were measured at the airway opening using 3 monitors, depending on the study phase (detailed below). Data were recorded directly from the NICU ventilator during ward care (SLE5000 infant ventilator; SLE UK, South Croydon, UK). The SLE5000 ventilator measures V_T using a hot wire anemometer flow sensor, with a manufacturer-reported V_{Te} range of 0.2-32.0 mL and ±8.0% accuracy. A respiratory function monitor (RFM) was in use during all surgeries (Florian; Acutronic, Hirzel, Switzerland). The Florian RFM uses the same hot wire anemometer as the SLE5000, has been widely validated in neonatal respiratory states,[11,17] but has no internal power source and thus is not suited to intrahospital transport. During transportation between the operating theatre and NICU, V_{Te} and pressure were recorded using a Ventcheck 101 RFM (Novametrix Medical Systems, Wallingford, Connecticut), a battery-powered handheld RFM designed for transport that uses a differential pressure pneumotach (V_T range, 0.25-35.0 mL; ±3.0% accuracy [manufacturer-supplied data]). For 2 months during the study period, the disposable Ventcheck pnuemotach was not available, and a Florian RFM with a UPS power supply was substituted (5 infants). All flow sensors had a deadspace of 1.0 mL,[18] and were calibrated to zero flow immediately before use, in accordance with the manufacturer's instructions.

Heart rate, respiratory rate, mean blood pressure, peripheral oxygen saturation (SpO_2), mainstream end-tidal carbon dioxide ($EtCO_2$), and fraction of inspired oxygen (FiO_2) were recorded when available with V_{Te} and pressure settings from the hospital's Philips MP80 monitor (Philips Healthcare, Eindhoven, The Netherlands). During surgery, respiratory support was provided with the Aisys Carestation (GE Healthcare, Madison, Wisconsin), which offers continuous V_{Te} monitoring from the proximal end of the ventilator circuit. These data were also recorded when available.

After intubation, data were recorded during 3 distinct periods. In the intraoperative period, the RFM flow sensor was incorporated into the circuit at the airway opening at intubation or on transfer to operating table. Data, including Aisys-displayed V_{Te}, were then recorded every 4 minutes until the completion of surgery. During transport between the NICU and OT, with the RFM in situ, neonates were supported by either a Neopuff infant resuscitator T-piece device (Fisher Paykel Healthcare, East Tamaki, New Zealand) or a 450-mL flow-inflating bag with manometer, at the discretion of the treating anesthetist. Data were collected every 1 minute during transport. During immediate postoperative NICU care, V_{Te} and pressure were recorded directly from the ventilator display every minute for 15 minutes after the neonates were returned to the NICU.

During all phases of the study, the settings and mode of respiratory support were at the discretion of the clinical team, who were blinded to the RFM values. One-minute intervals for data capture were chosen for the transport and NICU phases because of the shorter time periods.

Data Acquisition and Analyses

Continuous breath-to-breath digital acquisition of V_{Te} and pressure was not possible, owing to transport and the lack of digital output on the Ventcheck device. Thus, the displayed values for all variables were manually recorded onto a dedicated data sheet at each time point.

Intrasubject and intersubject descriptive statistics were generated for each phase of the study, including the proportion of V_{Te} values above, below, and within the 4.0-8.0 mL/kg range and the coefficient of V_{Te}, PIP, and physiological measures of variability. Descriptive comparison of V_{Te} variability during the 3 study phases was the primary outcome. Because data did not pass normality testing, differences in V_{Te} and other variables between phases were compared using the Mann-Whitney *U* test or the Kruskal-Wallis test (or equivalent if data were paired) and the Dunn post hoc test as indicated. Binary data were compared using the χ^2 or Fisher exact test as appropriate. The Bland-Altman technique was used to assess V_{Te} accuracy, bias, and reliability between the Aisys and the RFM. Statistical analysis was performed using Prism 6.05 (Graphpad Software, La Jolla, California). A P value < .05 was considered to indicate statistical significance.

Results

A total of 2597 paired V_{Te}, pressure and physiological data measurements were obtained (1972 intraoperatively, 250 during transport, and 242 during NICU care) from 26 infants. Demographic data are provided in **Table I**, and the enrollment process is illustrated in **Figure 1** (available at www.jpeds.com). Five infants were intubated before leaving the NICU, and 8 infants were extubated before leaving the operating theatre.