Current state of noninvasive, continuous monitoring modalities in pediatric anesthesiology

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Purpose of review
The last decades, anesthesia has become safer, partly due to developments in monitoring. Advanced monitoring of children under anesthesia is challenging, due to lack of evidence, validity and size constraints. Most measured parameters are proxies for end organ function, in which an anesthesiologist is actually interested. Ideally, monitoring should be continuous, noninvasive and accurate. This present review summarizes the current literature on noninvasive monitoring in noncardiac pediatric anesthesia.

Recent findings
For cardiac output (CO) monitoring, bolus thermodilution is still considered the gold standard. New noninvasive techniques based on bioimpedance and pulse contour analysis are promising, but require more refining in accuracy of CO values in children. Near-infrared spectroscopy is most commonly used in cardiac surgery despite there being no consensus on safety margins. Its place in noncardiac anesthesia has yet to be determined. Transcutaneous measurements of blood gases are used mainly in the neonatal intensive care unit, and is finding its way to the pediatric operation theatre. Especially CO₂ measurements are accurate and useful.

Summary
New techniques are available to assess a child’s hemodynamic and respiratory status while under anesthesia. These new monitors can be used as complementary tools together with standard monitoring in children, to further improve perioperative safety.

Keywords
bioimpedance, near-infrared spectroscopy, noninvasive monitoring, transcutaneous measurements

INTRODUCTION
Patient safety is the number one issue in anesthesiology. At present, anesthesia is absolutely safe in uncomplicated patients undergoing low-risk procedures, as improvement of monitoring modalities and anesthetics, and the preparation of the perioperative process have led to optimization of care. In general, intraoperative mortality has dramatically decreased in the last decades [1]. This overall safety has led to a change of the paradigm of anesthesia, from survival of the surgery and avoiding direct side effects into concepts based on quality of life and value-based health care. This requires a new view on monitoring to optimize organ preservation by controlling local oxygenation and metabolism.

In perioperative monitoring of pediatric patients, we face specific challenges, which postponed the development of appropriate age and size-related pediatric monitors. First, it is not always possible to get baseline measurements and some equipment is not validated for children or has size limitations. Moreover, there is no consensus on safety margins of some parameters, while goal directed monitoring in adults has already been established.

Due to rapid hemodynamic and respiratory changes under anesthesia, continuous and noninvasive monitoring would be favorable. Most parameters daily used in anesthesia are only proxies for end organ function. The brain is perhaps the most vulnerable, but also the least monitored organ. Due

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Curr Opin Anesthesiol 2020, 33:781–787
DOI:10.1097/ACO.0000000000000927

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to the development of encephalopathy in (ex)pre-term neonates requiring multiple surgeries, pediatric anesthesiologists are especially interested in brain perfusion [2]. We know that a short anesthetic in healthy children is harmless, but if this is still the case in high-risk neonates and infants undergoing multiple procedures remains unknown [3**]. It is unclear what exactly happens within the brain during anesthesia, due to changes in fluid status, cerebral perfusion pressure, CO2 pressure and unknown local factors.

The current review focuses on recent developments and current evidence on noninvasive monitoring in noncardiac pediatric anesthesia. We will concentrate on cardiac output (CO), near-infrared spectroscopy (NIRS) and transcutaneous blood gas analysis as monitors that may guide our interventions to optimize end organ function of our patients.

HEMODYNAMIC MONITORING

Blood pressure (BP) measured noninvasively with the oscillometry technique (NIBP) has a good correlation with intra-arterial BP (IABP), also in infants and neonates [4]. However, changing the site of measurement from the arm to another location may provide less reliable information. Large deviations are common when NIBP is measured from the leg or forearm in children under anesthesia, compared with arm NIBP. Leg NIBPs are usually lower than arm measurements in children, in contrast to higher leg NIBPs in adults. In children the soft, compliant pediatric arteries produce less augmentation of the signal than stiffer adult arteries. Also a reduced sympathetic tone and a relatively reduced blood volume in the lower limbs of small children may play a role [5*,6–8].

Continuous noninvasive BP can be measured with a finger cuff, measuring noninvasive finger arterial pressure (FINAP) by clamping the finger artery to a constant volume and varying the counter pressure [9,10]. With the Nexfin monitor (Table 1), FINAP is reconstructed into a brachial arterial pulse pressure waveform. In children, the FINAP was reliable, with a good level of agreement for DBP and mean arterial pressure between the Nexfin and IABP. However, underestimation of Nexfin SBP was observed [11,12].

The CNAP monitor (Table 1) provides beat-to-beat noninvasive pressure readings. In pediatric patients, the continuous BP readings were clinically useful. However, there is some variation in accuracy, especially with SBPs. Cuff placement was sometimes problematic, so further development in finger cuffs for children is necessary [14,15].

CARDIAC OUTPUT MEASUREMENTS

CO is the product of cardiac stroke volume (SV) and heart rate (HR). CO is measured by transpulmonary dilution techniques, requiring central venous catheterization [16,17]. Bolus thermodilution is still the most accepted reference method [18]. Less invasive techniques have become available, such as pulse contour cardiac output analysis, arterial pressure curve-based CO measurements, transesophageal Doppler (TED) and partial rebreathing of CO2. Transthoracic echocardiography or ultrasonic monitors are noninvasive, but noncontinuous measures [16,17,19–21].

Pulse contour analysis (PCA) of IABP waveforms can estimate CO continuously [17]. PCA can be measured noninvasively with devices such as the Nexfin monitor or Mobil-O-Graph (Table 1). Pediatric studies using this method are limited. The PCA-derived CO values of the Mobil-O-Graph were measured in awake adults and children at least 10 years of age, and showed to be comparable with two-dimensional echocardiography and ultrasonic monitors are noninvasive, but noncontinuous measures [16,17,19–21].

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At low CO values, PCA-derived data were higher than data from echocardiography. This type of CO measurement needs further refining in accuracy and precision, before it can be used in pediatric anesthesia.

Another technique of measuring CO continuously is based on the bioimpedance method. Bioimpedance cardiography measures changes in thoracic electrical bioimpedance during the cardiac cycle via electrodes on the skin, from which SV, and subsequently CO can be calculated [23]. Several devices are on the market measuring bioimpedance, electrical velocimetry or bioimpedance (Table 1).

Electrical velocimetry relates the maximum rate of change of impedance to peak aortic blood acceleration during the cardiac cycle. The change in orientation of the red blood cells in the aorta, from random during diastole (high-impedance state) to an aligned or parallel orientation during systole...
| Measurement of | Device name | Technology | Use in pediatric patients (literature) | Method |
|---------------|-------------|------------|----------------------------------------|---------|
| Cardiac output | Mobil-O-Graph ([I.E.M. GmbH, Stolberg, Germany]) | PCA | Zocalo et al. [22**] Only investigated in children of 10 years and older | Oscillometric cuff placed around the arm, measures peripheral BP, determines central BP waveform and quantifies several parameters including CO |
| Cardiac output | ICON ([Cardiotronic/ Osypka Medical, Inc, La Jolla, California, USA]) | Thoracic bioimpedance/Electrical cardiometry | King et al. [28] Cote` et al. [24] Observational studies in children 1 day to 19 years old | In neonates and small infants: 4 EKG electrodes placed on the left leg, left chest, left neck and forehead or cheek. Older patients: 2 EKG electrodes on the left chest and 2 on the left side of the neck |
| Cardiac output | Aesculon ([Osypka Medical GmbH, Berlin, Germany]) | Thoracic bioimpedance/Electrical velocimetry | Absolute CO values in children not reliable [Tomaske et al. [25]] | 2 EKG electrodes on the left chest and 2 on the left side of the neck |
| Cardiac output | NICOM (Cheetah Medical, Wilmington, Delaware, USA) | Transthoracic bioelectance | Not feasible in children <10 kg [Dubost et al. [31]; Sun et al. [30]] | A current injecting device (high frequency, 75 kHz alternating current) and 4 dual sensing electrodes, placed on the thorax |
| Cardiac output | IQ, model 101 ([Noninvasive Medical Technologies LLC, Auburn Hills, Michigan, USA]) | Thoracic bioimpedance | Martin et al. [13] | Prewired hydrogen electrodes on the skin, and 3 EKG electrodes on the precordium and each shoulder. A 100 kHz, 4 mA alternating current is passed through the thorax by the outer pairs of electrodes and the voltage is sensed by the inner pairs |
| Cardiac output | USCOM (USCOM Ltd, Sydney, New South Wales, Australia) | Doppler ultrasound, transthoracic | Intermittent measurement. Reliable measurement in children, when operated by trained user [Dhanani et al. [21]; Cattermole et al. [20]] | Transducer/probe placed on the chest in suprasternal position |
| Cardiac output | NICO ([Novametrix Medical Systems Inc, Wallingford, Connecticut, USA]) | Partial rebreathing of CO2 | Less accurate in patients ventilated with <300 ml tidal volume [Levy et al. [19]] | Via an ETT without leak |
| Continuous BP | Nexfin HD monitor ([BMEYE, Amsterdam, the Netherlands]) | FiNAP; finger volume clamp method | Accurate for continuous measurement of MAP in children, but sometimes difficult placement of finger cuff in small children [Lemson et al. [12]; Garnier et al. [11]] | Finger cuff with infrared photoplethysmography. Built-in physiological calibration method (Physiocal; BMEYE) to check and adjust the set point of the clamped artery every 80 heartbeats. Also measures CO with PCA |
| Continuous BP | CNAP monitor 500 ([CNSystems Medizintechnik, Graz, Austria]) | CNAP values represent the arterial pressure at the brachial artery | Studies in children ≥20kg. Sometimes difficult placement of finger cuff [Tobias et al. [15]; Kako et al. [14]] | Cuff around 2 adjacent fingers on the same side as an arm cuff; calibration with upper-arm oscillometric measurements |

BP, blood pressure; CO, cardiac output; ETT, endotracheal tube; FiNAP, finger arterial pressure; MAP, mean arterial pressure; PCA, pulse contour analysis.
(low-impedance state), causes changes in electrical conductivity and electrical impedance [24]. In pediatric patients studies showed agreement, but not consistently [25–27]. Observational studies with the ICON monitor in 402 children, ranging from preterm neonates to teenagers, showed that continuous cardiovascular parameter assessment was feasible during anesthesia for patients of all sizes and that it provided useful, real-time information regarding adverse hemodynamic changes and the response to interventions [24,28].

Bioreactance is the variation of the analysis in the frequency spectra of a delivered oscillating current that occurs when the current traverses the thoracic cavity. It is less susceptible to interference than bioimpedance [17,29]. NICOM CO values showed a good correlation and agreement with echocardiography during anesthesia in pediatric patients with normal heart anatomy, but no agreement in pediatric patients with a cardiac defect [30]. In children undergoing major abdominal surgery, the NICOM showed poor correlation between confidence interval values obtained by bioreactance and TED [31].

A meta-analysis of CO monitoring devices in adults found that no noninvasive device or technology was interchangeable with bolus thermodilution; the percentage of error was 42% for bioimpedance and 45% for noninvasive PCA, where a maximum of 30% percentage of error is considered acceptable [32]. Still, the noninvasive CO monitors could be interesting bedside monitors, as the percentage of error was similar to that of minimally invasive CO monitors, such as FloTrac (Edward Lifesciences Corp., Irvine, California, USA).

**NEAR-INFRARED SPECTROSCOPY**

Almost 30 years after the introduction of the first commercially available NIRS monitor the value of NIRS and its applicability in pediatric anesthesia are still a matter of debate.

NIRS is still misunderstood while a short introduction to its technical background would help to use it in the best interest of patients at risk of inadequate tissue oxygenation [33,34*,35]. NIRS provides blood flow independent real time information regarding regional tissue oxygenation (r-SO2), and the oxygen uptake/consumption balance. It should not be confused with pulse oximetry.

Cerebral NIRS monitoring has become a standard monitoring tool in many pediatric cardiac centers and neonatal ICUs. In noncardiac pediatric anesthesia, however, NIRS has not yet become part of the standard monitoring equipment, and the price of the disposables certainly requires careful patient selection.

Despite significant scientific efforts during the last two decades aiming at the definition of normal ranges [36,37] and lower safety margins [38–41] of cerebral r-SO2 in children, consensus regarding these important targets has not yet been reached. Many pediatric anesthesiologists have adopted common adult patient intervention limits like baseline r-SO2 –20% or an absolute value less than 55% [35]. Gómez-Pesquera et al. [42*] recently demonstrated the association of a decrease in cerebral r-SO2 of less than 20% and negative behavioral changes on postoperative day 7 in noncardiac pediatric patients.

Kamata et al. [43*] reported a decrease in cerebral r-SO2 values during laparoscopic surgery in children, not reaching awake baseline levels, while hemodynamic and respiratory parameters remained unchanged. Costerus et al. [44*] reported decreases in cerebral r-SO2 (≤10% from baseline) during neonatal thoracoscopic surgery and favorable neurodevelopmental outcome within 24 months despite severe intraoperative acidosis.

Two recent studies conducted in infants found no evidence of an effect of awake caudal [45*] and spinal [46] anesthesia on cerebral r-SO2.

**RECENT DEVELOPMENTS IN NEAR-INFRARED SPECTROSCOPY MONITORING**

The list of new applications of NIRS monitoring in pediatric anesthesiology is continuously growing.

Combined cerebral and peripheral (muscle) NIRS monitoring is a new trend, with some initial evidence of its capability to detect early stage centralization [47].

The calculation of fractional regional tissue oxygen extraction [FTOE = (SaO2 - r-SO2)/SaO2] [48], a composite parameter reflecting the regional oxygen delivery/consumption balance is also becoming increasingly used.

Jildénstål et al. [49*] found an acceptable level of agreement between frontal and occipital recordings of cerebral rSO2, introducing the possibility to apply NIRS during surgical procedures where the forehead is not available for sensor placement.

Neunhoeffer et al. [50] found a positive effect of red blood cell transfusion on FTOE and cerebral rSO2 in postsurgical infants, suggesting the feasibility of both parameters as transfusion triggers.

Smarius et al. [51*] observed a significant reduction in cerebral rSO2 induced by hyperextension of the neck during positioning for cleft palate repair surgery in children.

Lang et al. [52*] found initial evidence of additional value of perioperative cerebral NIRS monitoring as a measure of intracranial pressure in symptomatic pediatric hydrocephalus patients.
NEAR-INFRARED SPECTROSCOPY
DIRECTED HEMODYNAMIC MANAGEMENT

We recently developed a hemodynamic management algorithm using cerebral r-SO₂ as the single target parameter, using BP, PaCO₂, HR and SaO₂ as major contributing parameters [34*]. A preinduction awake baseline r-SO₂ is defined as the lowest acceptable value during the anesthetic. Our experience from several hundred patients has confirmed the feasibility of this approach.

TRANSCUTANEOUS BLOOD GAS ANALYSIS

The principles of transcutaneous blood gas analysis have already been described in the late fifties by Clark and Stow-Severinghaus [53,54]. Although continuous and noninvasive, it was prone to errors compared with simpler techniques such as pulse oximetry. As the introduction of user-friendly transcutaneous sensors, their use is increasing. Especially, measurement of CO₂ is reliable. This is particularly important due to the increase of video-assisted procedures. Insufflation increased. During an operation, changes in application [57] are necessary, before measurements can be interpreted safely. Nevertheless, due to improvements in sensor application [57*], its use perioperatively has increased. During an operation, changes in hemodynamics or fluid status and anesthetic agents as well as vasoactive medication could have effect on transcutaneous measurements by influencing the microcirculation, so doubts remain about the perioperative validity of measurements.

RECENT FINDINGS

Only few studies have been published on this subject. Nosovitch et al. [59] performed the first perioperative study in children in 2002. They concluded that of noninvasive measurements of CO₂, transcutaneous values were slightly more accurate than end-tidal measurements. Dullenkopf et al. [60] compared end-tidal and transcutaneous measurements of CO₂ in 60 children under general anesthesia and found no significant difference in accuracy between the two methods. Karlsson et al. [61] concluded on a relatively small group of neonates under general anesthesia that measurements where technically possible but not yet accurate.

Recently, Chandrakantan et al. [62**] compared end-tidal and transcutaneous CO₂ to venous blood gas values in children under 10 kg and showed that transcutaneous measured CO₂ has good correlation to venous values which are slightly better than standard end-tidal CO₂. May et al. [63*] reported similar results comparing single CO₂ values simultaneously obtained during arterial, venous, transcutaneous and end-tidal analysis in 47 children (mean age 13.4 ± 7.8 years old) with cystic fibrosis during anesthesia. Transcutaneous monitoring was more accurate and closer to PaCO₂ than capnography.

DISCUSSION

The ultimate monitor should be easy to set up and should provide the pediatric anesthesiologist of continuous, noninvasive, accurate, reproducible and real-time measurements. Ideally, this would display end organ function.

So far, this monitor has not yet been available. Some techniques, however, seem very promising. Regarding BP measurements and CO monitoring improvements are being made with regard to availability and accuracy in children. Further development of finger cuffs for smaller children is necessary. Although the bioimpedance technique seems very promising, drawbacks are that in young children the electrodes may be difficult to place, electrocautery induces loss of data, and arrhythmia or pleural effusion may limit its use [24,29,31]. Most importantly, more research needs to be conducted on the accuracy of the absolute CO values of these devices before it can be applied routinely during anesthesia in pediatric patients.
NIRS is not the holy grail, but it is the best currently available to continuously and noninvasively measure regional tissue-oxygenation and tissue-perfusion. Using the r-SO2 as the single outcome parameter in hemodynamic monitoring requires a paradigm shift in pediatric anesthesia toward tissue oxygenation, away from BP. Additional muscle NIRS monitoring may become the ultimate addition to ensure adequate oxygenation of all tissues.

Transcutaneous measurements are complimentary to, and not a replacement of other modalities. It is, however, a great advantage that noninvasively and continuously measurements are now available. But the gold standard for assessment of gas exchange remains blood gas analysis, and for correct tube placement capnography. In the near future more studies are required confirming validity in children under anesthesia and in areas where these measurements can contribute to safety such as laryngeal surgery, video-assisted procedures and procedural sedation.

CONCLUSION
Small steps are being made to improve the monitoring modalities in pediatric anesthesia as new techniques are available to assess a child’s hemodynamic and respiratory status while anesthetized. As perioperative safety is high nowadays, we face the challenge to take these small steps and use these new monitors as complementary tools together with standard monitoring in benefit of the most vulnerable patients.

Acknowledgements
The authors wish to thank Wichor Bramer, PhD, from the Erasmus MC Medical Library for developing and updating the search strategies, and Gall Snoones, MD, from the Department of Anesthesiology, Erasmus MC Sophia Children’s Hospital, for critical appraisal of the article.

Financial support and sponsorship
None.

Conflicts of interest
There are no conflicts of interest.

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•• of outstanding interest

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