References

1. Pollack CV Jr, Reilly PA, Eikelboom J, *et al*. Idarucizumab for dabigatran reversal. *N Engl J Med* 2015; **373**: 511–20
2. Eikelboom JW, Quinlan DJ, van Ryn J, Weitz JI. Idarucizumab: the antidote for reversal of dabigatran. *Circulation* 2015; **132**: 2412–22
3. Lang T, Bauters A, Braun SL, *et al*. Multi-centre investigation on reference ranges for ROTEM thromboelastometry. *Blood Coagul Fibrinolysis* 2005; **16**: 301–10
4. Reilly PA, Lehr T, Haertter S, *et al*. The effect of dabigatran plasma concentrations and patient characteristics on the frequency of ischemic stroke and major bleeding in atrial fibrillation patients: the RE-LY Trial (Randomized Evaluation of Long-Term Anticoagulation Therapy). *J Am Coll Cardiol* 2014; **63**: 321–8
5. Hankey GJ, Eikelboom JW. Dabigatran etexilate: a new oral thrombin inhibitor. *Circulation* 2011; **123**: 1436–50
6. van Ryn J, Stangier J, Haertter S, *et al*. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost* 2010; **103**: 1116–27

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Does the plethysmographic variability index predict fluid responsiveness in mechanically ventilated children? A meta-analysis

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Editor—The plethysmographic variability index (PVI), a dynamic index of preload dependence based on the respiratory variations in the pulse oximetry plethysmographic waveform amplitude, is a reliable and non-invasive predictor of fluid responsiveness in mechanically ventilated adults.[1] However, few studies in the literature have investigated the ability of the PVI to predict the response to volume expansion in the paediatric population, with conflicting results.[2] The goal of this meta-analysis was to summarize available evidence about the diagnostic accuracy of the PVI for the prediction of fluid responsiveness in children under mechanical ventilation.

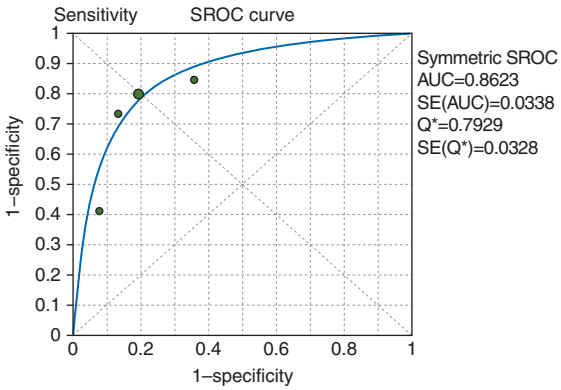

Fig 1 Summary receiver operating characteristic (SROC) curve of the plethysmographic variability index to predict fluid responsiveness in mechanically ventilated children. Filled circles represent each study included in the meta-analysis. AUC, area under curve; SE, standard error.

We searched the Medline, Google Scholar, and Cochrane databases, from inception to April 2016, to identify studies published as full-text articles in indexed journals that investigated the diagnostic accuracy of the PVI in predicting fluid responsiveness in mechanically ventilated children. The search terms used were as follows: 'pleth' or 'plethysmography'; 'child' or 'adolescent' or 'infant'; 'variation' or 'variability'; and 'index' or 'indices'. All statistical analyses were performed using Meta-Disc software version 1.4 (Ramon y Cajal Hospital, Madrid, Spain) for Windows. We calculated pooled values of diagnostic odds ratio, sensitivity, and specificity of PVI to predict the response to fluid challenge, using a random-effects model. A summary receiver operating characteristic curve was drawn to define the ability of PVI to discriminate between responders and non-responders to fluid challenge. Heterogeneity between studies was assessed using the Cochran's Q and I^2 tests. All values were reported as the point estimate with 95% confidence interval (CI).

Four studies, with a total of 144 patients and 187 fluid boluses, were included in the meta-analysis.[3–6] The mean responder rate was 48%. All studies were carried out in the operating theatre. The mean threshold value for the identification of responders to volume expansion was 14% (SD 3). The area under the summary receiver operating characteristic curve of PVI to predict fluid responsiveness was 0.86 (Fig. 1). The pooled sensitivity, specificity, and diagnostic odds ratio of PVI for the overall population were 72% (95% CI 62–81), 81% (95% CI 71–88), and 14 (95% CI 7–31), respectively. No significant statistical heterogeneity between the studies was found for specificity or diagnostic odds ratio ($P>0.1$; $I^2<50\%$). Conversely, a significant heterogeneity was found for sensitivity ($P=0.02$; $I^2=69\%$). Given the low number of studies included in this work, meta-regression analysis to explore the possible sources of clinical or methodological heterogeneity between studies was not performed.

In summary, this meta-analysis suggests that the PVI could be an accurate predictor of fluid responsiveness in children under mechanical ventilation in the operating theatre. In the future, this non-invasive haemodynamic monitoring tool could be incorporated into an intraoperative fluid management algorithm in the paediatric population. However, given the low number of studies and participants and the heterogeneity among studies in terms of sensitivity, additional studies are required to confirm our findings before recommending the PVI for routine assessment of fluid responsiveness in children.

Declaration of interest

None declared.

References

1. Chu H, Wang Y, Sun Y, Wang G. Accuracy of pleth variability index to predict fluid responsiveness in mechanically ventilated patients: a systematic review and meta-analysis. *J Clin Monit Comput* 2016; **30**: 265–74
2. Gan H, Cannesson M, Chandler JR, Ansermino JM. Predicting fluid responsiveness in children: a systematic review. *Anesth Analg* 2013; **117**: 1380–92
3. Pereira de Souza Neto E, Grousson S, Duflo F, *et al*. Predicting fluid responsiveness in mechanically ventilated children under general anaesthesia using dynamic parameters and transthoracic echocardiography. *Br J Anaesth* 2011; **106**: 856–64
4. Renner J, Broch O, Gruenewald M, *et al*. Non-invasive prediction of fluid responsiveness in infants using pleth variability index. *Anaesthesia* 2011; **66**: 582–9
5. Byon HJ, Lim CW, Lee JH, *et al*. Prediction of fluid responsiveness in mechanically ventilated children undergoing neurosurgery. *Br J Anaesth* 2013; **110**: 586–91
6. Julien F, Hilly J, Sallah TB, *et al*. Plethysmographic variability index (PVI) accuracy in predicting fluid responsiveness in anesthetized children. *Paediatr Anaesth* 2013; **23**: 536–46

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Improved postoperative oxygenation after antagonism of moderate neuromuscular block with sugammadex *versus* neostigmine after extubation in 'blinded' conditions

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Editor—Neuromuscular blocking agents are routinely used during general anaesthesia to optimize intubation and improve surgical conditions. For example, we recently showed that a deep neuromuscular block (NMB) improves the quality of the surgical field in retroperitoneal laparoscopic surgery.[1] The persistence of some level of NMB [residual relaxation defined by a train-of-four (TOF) ratio <0.9] during and after extubation is an independent risk factor for postoperative pulmonary complications, with hypoxaemia as most the frequent event.[2 3] In order to assess whether the practice of NMB antagonism has an effect on residual NMB and oxygenation levels in the postanaesthesia care unit (PACU), we conducted a multicentre, double-blind, randomized controlled trial (with acronym NEUROPA) comparing the effect of antagonism of a moderate NMB (TOF one to two twitches) with sugammadex 2 mg kg^{-1} *vs* neostigmine 2.5 mg on oxygen saturation (Sp_{O_2}) values in the PACU. The use of neostigmine 1–2.5 mg is currently the standard of practice in the two hospitals where this study was conducted (Leiden University Medical Center, Leiden and HagaZiekenhuis, The Hague, The Netherlands). In order to obtain an indication of the oxygenation status of the patients in the PACU without the confounding effects of supplemental oxygen, the application of an oxygen mask was not allowed unless Sp_{O_2} was <94%. The study was registered (Clinical Trials.gov NCT02243943), approved by the local ethics committees, and all patients gave written informed consent before participation. All patients received total i.v. anaesthesia (propofol, sufentanil, and rocuronium); the level of NMB was kept at one to two twitches in the TOF. After antagonism, the attending anaesthetist was blinded to the TOF monitor, and extubation was based on clinical grounds (head lift, hand grip, open eyes, tongue protrusion, etc.).

One hundred patients were randomized, with 50 patients in each group. The attending anaesthetist decided that after antagonism, eight patients required one additional neostigmine dose of 1 mg; three others received a dose of sugammadex after their initial neostigmine dose. None of the patients who initially received sugammadex required additional treatment. The mean T4/T1 ratio (95% confidence interval) at extubation was 0.74 (0.71–0.83) in the neostigmine group *vs* 0.99 (0.98–1.00) in the sugammadex group ($P<0.0001$). Thirty-five (70%) patients treated with neostigmine had a TOF ratio <0.9 upon extubation *vs* two (4%) of the patients treated with sugammadex. The lowest Sp_{O_2} in the PACU was 93.3 (91.9–94.7)% in the neostigmine group *vs* 96.8 (96.1–97.4)% in the sugammadex group ($P<0.0001$). Figure 1 shows the individual lowest saturation value in the PACU *vs* TOF ratio at extubation. In the sugammadex group, 90% of the patients were in the upper right quadrant of the graph (TOF ratio of >0.9 combined with lowest saturation ≥94%) *vs* 16% of patients treated with neostigmine. In the PACU, no significant differences in sedation and pain scores were observed. No adverse events occurred.

Low Sp_{O_2} values are not uncommon in the PACU and are related to multiple factors, including the residual effects of opioids and anaesthetics, type of surgery, patient characteristics,