# Editorial

## Do we need to monitor cardiac output in spontaneously breathing patients?

Optimising cardiac output is a major goal during anaesthesia and in the intensive care unit (ICU) in order to provide optimal oxygen delivery and prevent organ malfunction or even failure. It has been suggested that early goal-directed haemodynamic optimisation, for instance by continuously measuring and optimising stroke volume, may lead to a decreased infection rate, fewer unwanted cardiac events and faster recovery of bowel function, with a reduction in postoperative morbidity [1–4]. However, the recommendation of the routine use of oesophageal Doppler in major surgery continues to generate ongoing discussion [5–8].

A survey by Cannesson et al., of North American and European anaesthesiologists' intra-operative management of patients undergoing high-risk surgery, revealed that only approximately one third of the respondents in both Europe and the USA used cardiac output monitoring [9]. Moreover, only 30% of the European anaesthesiologists and 5% of the American anaesthesiologists followed a pre-defined optimisation protocol [9]. This survey demonstrates two things: first, we have to provide more convincing evidence that minimal invasive cardiac output monitoring tools embedded in pre-defined optimisation protocols are accurate; and second, we are too slow transferring already available evidence-based practice in daily routine.

Whilst the discussions continue about patients requiring controlled ventilation during anaesthesia or in the ICU, what about a haemodynamic monitoring strategy or even an optimisation protocol in conscious patients, before surgery, in the post-anaesthesia care unit (PACU) or in the regular ward? In 1999, Goldhill et al. described the management and outcome of patients admitted from the ward to the ICU who had not undergone surgery within 24 hours of admission [10]. One third of the identified patients underwent cardiopulmonary resuscitation before their admission to the ICU, and most of these patients had received oxygen and had their oxygen saturation measured in combination with arterial blood gas sampling. Two thirds had an oxygen saturation < 90%. The overall in-hospital mortality was 58% [10]. A few years later, Story et al. supported these data with their study investigating the effect of a combined critical care outreach and acute pain service on postoperative morbidity and mortality [11]. They were able to demonstrate that the incidence of serious adverse events decreased from 23 events per 100 patients to 16 events per 100 patients, associated with a reduction in 30-day mortality from 9% to 3% [11]. In a more recent review from 2011 regarding the peri-operative care of surgical patients, the authors stated that there was a problem with pre-operative risk assessment, intra-operative monitoring protocols and individualised postoperative care strategies: only 22% of patients identified as high-risk were cared for in a critical care unit postoperatively, and 48% of high-risk patients who died never went to an ICU [12]. Data from the recent European EuSOS study revealed that over 70% of patients who did not survive non-cardiac surgery were never admitted to the ICU [13]. In summary, these studies identify at least two problems: first, general deterioration is often insufficiently recognised, despite partial documentation; and second, intervention is often initiated too late. This raises questions over our strategies for (i) allocation of critical care resources and (ii) therapy on the ward, in particular the feasibility of advanced haemodynamic monitoring and adequate optimisation/resuscitation protocols in spontaneously breathing patients.

Spontaneously breathing patients in whom such monitoring would be most useful are those arriving in our emergency departments with trauma, an acute abdomen or bleeding, where the primary goals are rapid identification of risk and adequate resuscitation [14]. It is well known that emergency surgery is associated with a dramatically increase in mortality [15] and that the capacity for ICU admission, even though differing highly between countries [16], is often very limited [14]. A considerable number of these emergency patients are now being treated without the need for general anaesthesia, due to interventional methods that allow these procedures to be performed under sedation or regional anaesthesia [15, 17]. Indeed, the use of less invasive procedures (e.g. transfemoral aortic valve implantation or endovascular aneurysm repair) continues to expand, and anaesthetists or intensivists are likely to find themselves also caring for an increasing number of elective high-risk patients receiving sedation with preserved spontaneous breathing [18, 19]. There is an urgent need for an expert anaesthesia team in these procedures, to provide the highest standard of safety with regard to: i) performance of sedation; ii) haemodynamic stability and oxygen delivery; iii) resuscitation; and iv) availability of experienced airway management.

Many spontaneous breathing patients after high-risk procedures are treated in a PACU or intermediate care unit, where detection of intravascular hypovolaemia by using promising dynamic variables for detection of fluid responsiveness, recommended for use in ICU and during anaesthesia, is hampered by the lack of controlled ventilation. Thus, even in the ICU, only a very low minority of patients meet the validity criteria for functional haemodynamic monitoring [20]. Therefore, studies on volume assessment and preload reserve in spontaneous breathing patients are both relevant and timely. In this issue of *Anaesthesia*, O`Loughlin and co-workers describe how they evaluated the ability of minimally/non-invasive cardiac output monitoring technologies to detect hypovolaemia caused by venesection in spontaneous breathing healthy subjects [21]. The authors confirmed that clinical signs and commonly used haemodynamic variables such as systolic blood pressure or heart rate are insufficient measures of blood loss. Whereas systolic blood pressure did not correlate with blood loss at all, a significant increase in heart rate occurred, though it was often delayed, owing to autonomic regulation mechanisms' masking the clinically significant hypovolaemia. However, significant changes in stroke volume, measured by different devices, indicated blood loss earlier (LIDCO™ after 2.5% blood loss; USCOM after 7.5%, CardioQ™ and FlowTrac after 12.5% blood loss) than routine heart rate monitoring (after 17.5% blood loss) and non-invasive blood pressure monitoring. Despite the small sample size, O`Loughlin et al.'s study highlights the potential of minimally invasive haemodynamic monitoring technologies to track changes in stroke volume (i.e. cardiac output) due to changes in intravascular volume status. Besides the technology evaluated in O`Loughlin et al.'s study, other non-invasive monitoring platforms are also currently available, offering the ability to estimate stroke volume, cardiac output and dynamic variables of fluid responsiveness continuously on the basis of a arterial blood pressure tracing measured by use of an inflatable finger cuff (ClearSight, Edwards Lifesciences, USA; CNAP® HD, CNSystems, Austria). These completely non-invasive systems, in particular, may play a more important role in the future with regard to advanced haemodynamic monitoring in spontaneously breathing patients not scheduled for a high-technology area such as an ICU. Even though there is still ongoing debate about the reliability of these technologies [22, 23], they may play an interesting role, because they are easy and fast to install without needing great expertise.

Therefore, the study of O`Loughlin et al. is of relevant interest. The authors state correctly that the different monitoring devices may aid in detection of blood loss in conscious patients. However, the question remains whether these monitoring tools are yet the ones we need. Is detection of true or relative hypovolaemia by a single parameter really useful and relevant in a clinical setting? All devices assume to measure and track changes in stroke volume due to hypovolaemia and resuscitation. However, O`Loughlin et al.'s study demonstrated a distinct methodological variability between the

 

different devices, questioning at least the accuracy and precision of some of them. For example, mean values of stroke volume at baseline ranged from 90.8 ml (CardioQ) to 138.9 ml (FlowTrac) in the same healthy population. On the other hand, ROC analysis revealed that optimal cut-off points of stroke volume decrease for the detection of significant blood loss (> 10%) ranged from 7% (–7.4 ml; LIDCO) to 12.8% (–10.7 ml; CardioQ). This highlights a clinical dilemma using these measurements, because these variations may diminish their clinical utility. From a statistical point of view, we need exact measures of absolute stroke volume or cardiac output compared with a clinical accepted gold standard. From a clinical point of view, it seems acceptable to base pre-defined haemodynamic optimisation protocols on monitoring tools that are at least able to track changes in stroke volume or cardiac output accurately. Whether mathematical statistical assistance systems that might be capable of including more than one input parameter (e.g. by using fuzzy logic) help in detecting hypovolaemia is another interesting question [24]. These systems may further increase the accuracy of the available monitoring techniques and perhaps enable automatic correction for different devices in the future as well.

The detection and early treatment of true or relative hypovolaemia, and consequently occult hypoperfusion, by the use of advanced haemodynamic monitoring devices may lead to fewer postoperative complications and even perhaps a reduction in hospital stay and the overall cost of peri-operative care. However, at present, the direct costs of these systems are relatively high, ranging between about £60 (€76; $97) and £150 (€189; $241) per patient, depending on the quantity ordered. Therefore, it is self-evident for the moment that such systems cannot be used unselectively. From the perspective of cost-effectiveness, it has been shown for elderly patients with hip fracture that a goal-directed fluid therapy concept enables saving costs and increases quality adjusted life years [25]. Still, it is crucial to start haemodynamic optimisation early and before organ failure occurs [26].

Hence, it is our task for the future to work on concepts for the early identification of patients at risk. Further, we have to demand the development of monitoring techniques as well as strategies and optimisation protocols, so that our patients are most likely to benefit from such advanced haemodynamic monitoring tools, especially during the entire peri-operative care period. In this context, the study of O`Loughlin et al. paves the way for future haemodynamic optimisation concepts based on minimal invasive monitoring tools.

## Competing interests

Both authors have a clinical and research interest in haemodynamic monitoring and have received research funding, by provision of equipment, from Edwards Lifesciences and Pulsion Medical Systems. JR has received speaking fees or travel expenses from Edwards Lifesciences.

**M. Gruenewald**
**J. Renner**
*Associate Professors of Anaesthesiology*
*Department of Anaesthesiology and Intensive Care Medicine, University Hospital Schleswig Holstein, Campus Kiel*
*Kiel, Germany*
*Email: matthias.gruenewald@uksh.de*

## References

1. Dalfino L, Giglio MT, Puntillo F, Marucci M, Brienza N. Haemodynamic goal-directed therapy and postoperative infections: earlier is better. A systematic review and meta-analysis. *Critical Care* 2011; **15**: R154.
2. Giglio MT, Marucci M, Testini M, Brienza N. Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: a meta-analysis of randomized controlled trials. *British Journal of Anaesthesia* 2009; **103**: 637–46.
3. Corcoran T, Rhodes JE, Clarke S, Myles PS, Ho KM. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesthesia and Analgesia* 2012; **114**: 640–51.
4. Arulkumaran N, Corredor C, Hamilton MA, et al. Cardiac complications associated with goal-directed therapy in high-risk surgical patients: a meta-analysis. *British Journal of Anaesthesia* 2014; **112**: 648–59.
5. Ghosh S, Arthur B, Klein AA. NICE guidance on CardioQ™ oesophageal Doppler monitoring. *Anaesthesia* 2011; **66**: 1081–3.
6. Minto G, Struthers R. Oesophageal Doppler monitoring: costly and supported by weak evidence. *Anaesthesia* 2012; **67**: 426–7.
7. Singer M. Oesophageal Doppler monitoring: a not-so-NICE editorial. *Anaesthesia* 2012; **67**: 428–30.
8. Morris C. Oesophageal Doppler monitoring, doubt and equipoise: evidence based medicine means change. *Anaesthesia* 2013; **68**: 684–8.
9. Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A. Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. *Critical Care* 2011; **15**: R197.
10. Goldhill DR, White SA, Sumner A. Physiological values and procedures in the 24 h before ICU admission from the ward. *Anaesthesia* 1999; **54**: 529–34.

11. Story DA, Shelton AC, Poustie SJ, Colin-Thome NJ, McNicol PL. The effect of critical care outreach on postoperative serious adverse events. *Anaesthesia* 2004; **59**: 762–6.
12. Findlay G, Goodwin A, Protopapa K, Smith N, Manson M. *Knowing the Risk. A Review of the Peri-operative Care of Surgical Patients*. London: National Confidential Enquiry into Patient Outcome and Death, 2011. http://www.ncepod.org.uk/2011report2/downloads/POC_fullreport.pdf (accessed 28/10/2014).
13. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012; **380**: 1059–65.
14. Gray LD, Morris CG. Organisation and planning of anaesthesia for emergency surgery. *Anaesthesia* 2013; **68**(Suppl 1): 3–13.
15. Stoneham M, Murray D, Foss N. Emergency surgery: the big three–abdominal aortic aneurysm, laparotomy and hip fracture. *Anaesthesia* 2014; **69** (Suppl 1): 70–80.
16. Wunsch H, Angus DC, Harrison DA, et al. Variation in critical care services across North America and Western Europe. *Critical Care Medicine* 2008; **36**: 2787–93, e1–9.
17. Ellard L, Djaiani G. Anaesthesia for vascular emergencies. *Anaesthesia* 2013; **68**(Suppl 1): 72–83.
18. Hutchinson N. Sedation vs general anaesthesia for the high-risk patient–what can TAVI teach us? *Anaesthesia* 2011; **66**: 965–8.
19. Wong GT, Irwin MG. EVAR fever: minimally invasive, maximally inclusive? *Anaesthesia* 2012; **67**: 351–4.
20. Mahjoub Y, Lejeune V, Muller L, et al. Evaluation of pulse pressure variation validity criteria in critically ill patients: a prospective observational multicentre point-prevalence study. *British Journal of Anaesthesia* 2014; **112**: 681–5.
21. OLoughlin E, Ward M, Crossley A, Hughes R, Bremner A, Corcoran T. The evaluation of minimally invasive monitors to detect hypovolaemia in conscious patients: a proof of concept study. *Anaesthesia* 2015; **70**: 142–9.
22. Broch O, Renner J, Gruenewald M, et al. A comparison of the Nexfin® and transcardiopulmonary thermodilution to estimate cardiac output during coronary artery surgery. *Anaesthesia* 2012; **67**: 377–83.
23. Taton O, Fagnoul D, De Backer D, Vincent JL. Evaluation of cardiac output in intensive care using a non-invasive arterial pulse contour technique (Nexfin®) compared with echocardiography. *Anaesthesia* 2013; **68**: 917–23.
24. Bardossy G, Halasz G, Gondos T. The diagnosis of hypovolemia using advanced statistical methods. *Computers in Biology and Medicine* 2011; **41**: 1022–32.
25. Bartha E, Davidson T, Hommel A, Thorngren KG, Carlsson P, Kalman S. Cost-effectiveness analysis of goal-directed hemodynamic treatment of elderly hip fracture patients: before clinical research starts. *Anesthesiology* 2012; **117**: 519–30.
26. Kern JW, Shoemaker WC. Meta-analysis of hemodynamic optimization in high-risk patients. *Critical Care Medicine* 2002; **30**: 1686–92.

doi:10.1111/anae.12951

# Editorial

## Tramadol – the Marmite™ drug

In this issue of *Anaesthesia*, Stevens et al. [1] provide more evidence for the complexity of tramadol usage. Tramadol was only licensed in the UK 30 years ago, yet in its short lifetime it has attracted a disproportionate amount of attention. From being relatively unknown outside the realms of anaesthesia and pain management, it now not only divides opinion within our specialty but has generated a real public awareness; it was held partly responsible for a number of collisions that occurred during professional cycling races in 2014 [2] and features in the title of controversial comedian Frankie Boyle's Channel 4 series *Tramadol Nights* [3]. It is therefore timely that we re-evaluate its use in anaesthesia, analgesia and peri-operative medicine.

### Pharmacology of tramadol

Tramadol hydrochloride is a synthetic analgesic that acts as a non-selective μ-, κ- and δ-opioid receptor agonist, blocking ascending pain signals as well as altering the cortical perception of pain by inhibiting the re-uptake of serotonin and noradrenaline. This re-uptake inhibition may also play a role in modulating descending pain pathways in the spinal cord [4]. Although classified as an opioid, only about 30% of tramadol's activity can be reversed with naloxone [4], and it is these non-opioid actions that set tramadol apart from other drugs. Minimal respiratory depression

 