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COMMENTARY

Shedding light on perioperative hemodynamic monitoring

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Abstract
Given the number of clinical studies and meta-analyses investigating the impact of cardiac output-guided hemodynamic management on the postoperative outcome of patients undergoing high-risk surgery, clinicians should already have a fair idea of the clinical and economic benefits. However, this is still a matter of debate, there are still large outcome studies going on, and surveys and audits have shown that clinical adoption remains low. Rational patient selection, more affordable monitoring solutions, and the personalization of therapeutic strategies are desirable to ensure that cardiac output monitoring adds value and becomes part of the routine anesthesia management of high-risk surgical patients.

Keywords Perioperative medicine · Hemodynamic monitoring · Blood pressure · Cardiac output · Fluid management

In a recent article published in Nature [1], more than 800 scientists called for "a stop to the use of p values in the conventional dichotomous way to decide whether a result refutes or supports a scientific hypothesis". They highlighted that "statistics often lead scientists to deny differences that those not educated in statistics can plainly see".

An example of a plainly visible but statistically insignificant difference is shown in Fig. 1, reproduced from the multicenter OPTIMISE trial published in 2014 [2]. In patients undergoing major abdominal surgery, cardiac output-guided hemodynamic management led to a 16% relative reduction in a composite outcome of postoperative complications and 30-day mortality. This reduction did not reach statistical significance ($p = 0.07$). Neither did the reduction in mortality from 11.6 to 7.7% at 180 days (Fig. 1). As a result, the value of cardiac output-guided hemodynamic management has been questioned and another, bigger, resource-demanding and time-consuming trial is now ongoing (optimiseii.org).

When looking more closely at the results of the OPTIMISE trial, one may actually question the need for another trial for the following reasons:

1. The reduction in postoperative morbidity and death was 20% ($p = 0.04$) after adjustment for non-compliance. This sub-group analysis was pre-specified and is justified by the fact that a hemodynamic strategy cannot be of any benefit if it is not adopted.
2. It reached 41% ($p < 0.01$) after excluding the first 10 patients per hospital. This subgroup analysis was also pre-specified and takes into account the inevitable learning curve when using a new hemodynamic monitor and following a new hemodynamic protocol.
3. The above-mentioned clinical benefits were associated with £400 savings/patient [3].
4. The mortality cumulative curves were visually divergent (Fig. 1).
5. The meta-analysis of 38 randomized controlled trials, published together with the results of OPTIMISE [2], concluded that cardiac output-guided hemodynamic management reduces postoperative morbidity (risk ratio 0.77, $p < 0.001$).
6. Finally, the recent re-analysis of OPTIMISE data using a Bayesian approach [4] led to the non-dichotomous conclusion that "the probability that the intervention decreased postoperative complications and death ranged between 96.9 and 99.5%".

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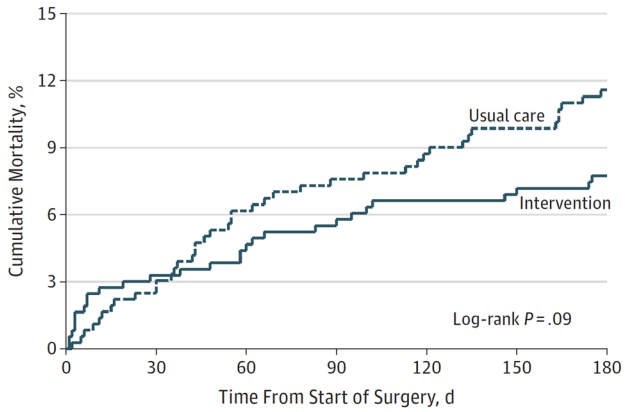

Fig. 1 Cumulative mortality curves comparing cardiac output-guided hemodynamic management (intervention) to routine management (usual care). From [2] with permission. They show a non-significant survival benefit at day 180 in the Intervention group. Specifically, the p value was 0.09, which means that the probability the "visible" difference was related to the intervention was 91%. In this context, concluding that the intervention lacks benefit seems questionable

Therefore, clinicians should already have a fair idea of the clinical benefits of cardiac output-guided hemodynamic management during high-risk surgery. And we believe they may be able to choose in which group of Fig. 1 they would like to belong to if they were a patient.

However, despite these data and official recommendations from several anesthesia societies, surveys and audits have shown that the clinical adoption of cardiac output-guided hemodynamic management remains low [5]. Barriers to adoption include the lack of clarity regarding which patients would benefit the most, and which monitoring tools and hemodynamic targets should be used. The cost of hemodynamic equipment is also an obstacle to wide hospital adoption.

1 Patient selection: keep it rational

The likelihood to develop postoperative complications depends on co-morbidities (patient risk) and on the surgical procedure itself (surgical risk). Several algorithms, taking into account both factors, have been developed to predict the probability of specific post-operative complications in the individual patient. The American College of Surgeons (ACS) predictive algorithm was developed using data collected from over 4.3 million operations from 780 hospitals. It has the major advantage to be freely accessible online (https://riskcalculator.facs.org/RiskCalculator). Patients at high risk to develop complications are those who may benefit the most from hemodynamic optimization (Fig. 2).

2 Cardiac output monitoring: keep it easy

The number of technical options to monitor cardiac output dramatically increased over the last decade, from bioimpedance tracheal tubes to bioreactance electrodes, and minimally or even non-invasive pulse wave analysis methods [6, 7]. Although first clinical evaluations were done with the esophageal Doppler, anesthetists have now a clear preference for uncalibrated pulse contour methods. They were used by around ¾ of anesthetists who were monitoring cardiac output in the large (> 45,000 patients) EUSOS study [8]. A recent meta-analysis of randomized controlled trials done with uncalibrated pulse contour methods in patients undergoing major surgery concluded to a significant improvement in postoperative outcome [9].

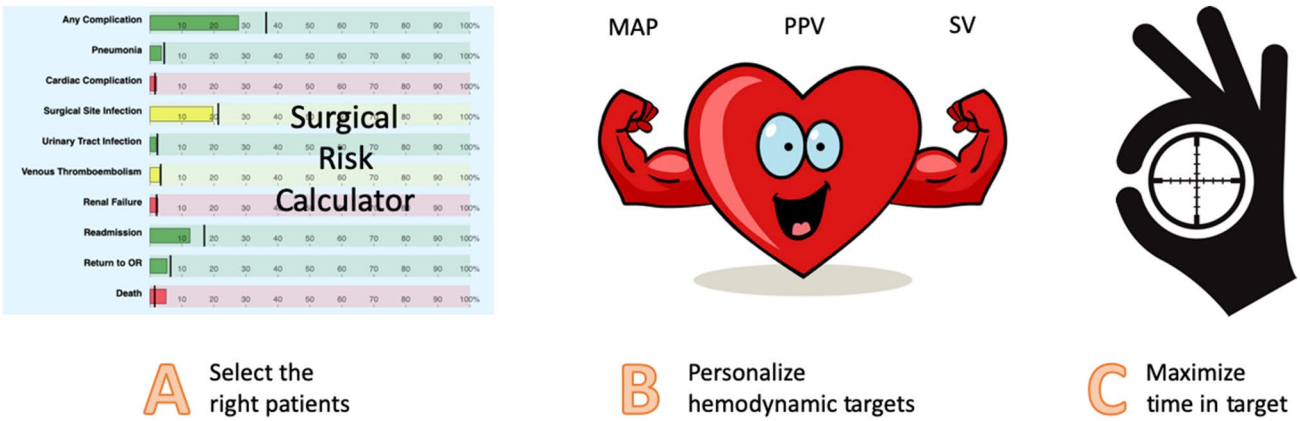

Fig. 2 The ABC of perioperative hemodynamic management

3 Hemodynamic targets: keep them personal

The selection of hemodynamic targets remains an ongoing debate but there is a consensus regarding the fact that (1) both blood pressure and flow are key determinants of organ perfusion and function (2) hemodynamic therapy should be tailored to individual needs [10]. For instance, fluid boluses should not be administered to fluid non-responders and, in this respect, dynamic variables (e.g. pulse pressure variation) may help to prevent unjustified fluid loading (Fig. 2). Preoperative hemodynamic profiles vary among individuals depending on demographic, biometric, clinical and metabolic factors [11]. Using pre-operative personal hemodynamic profiles to define perioperative target values is an emerging concept [12]. Pre-operative profiles are now easier to determine, thanks to ambulatory blood pressure monitoring techniques and new methods enabling clinicians to spot-check resting cardiac output values during the pre-operative visit or on the surgical ward the day before surgery. Futier et al. [13] conducted the first randomized controlled trial investigating the impact of maintaining intraoperative systolic blood pressure close to personal values (measured at rest days before surgery). They reported a significant decrease in postoperative organ dysfunction. Saugel et al. (clinicaltrials.gov: NCT02834377) have recently completed a similar study where personal cardiac output values measured the day before surgery are used as target values during the surgical procedure. Results should be published later this year. In any case, to ensure that hemodynamic variables remain within the individualized target range, visual decision support tools are now available and are to be recommended [14, 15].

4 The cost: keep it reasonable

The cost of hemodynamic monitoring technologies is another barrier to wide hospital adoption. A fair evaluation of the potential return on investment must balance the costs of the equipment with savings associated with the expected reduction in postoperative morbidity and hospital length of stay. Several studies have demonstrated that cardiac-output guided hemodynamic management may be cost saving [3]. In addition, more affordable solutions, including reusable sensors and unlimited usage plans, are becoming available. They are increasingly adopted by large medical institutions in order to cut expenses and increase the number of patients who may benefit from cardiac output monitoring at the same time.

In summary, a significant body of evidence already supports the clinical and economic value of cardiac output-guided hemodynamic management during high-risk surgery. Rational patient selection, more affordable monitoring solutions, and the personalization of therapeutic strategies are desirable to ensure it becomes part of the routine anesthesia management of high-risk surgical patients.

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Compliance with ethical standards

Conflict of interest FM is the founder and managing director of MiCo, a Swiss consulting firm. MiCo does not sell any medical products and FM does not own shares nor receive royalties from any medtech company. EF declares consulting fees from Drager Medical, GE Healthcare, Edwards Lifesciences, and Orion Pharma, and lecture fees from Fresenius Kabi and Getinge. BS is a member of the medical advisory board and received honoraria for giving lectures and refunds of travel expenses from Pulsion Medical Systems. BS received institutional research grants, unrestricted research grants, and refunds of travel expenses from Tensys Medical Inc. BS received honoraria for giving lectures and refunds of travel expenses from CNSystems. BS received research support from Edwards Lifesciences.

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